Alice M. Hunt

Chloroform Anæsthesia

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WITH A FOREWORD

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FOREWORD.

Not many years ago it would have been considered an anomaly, perhaps even an intrusion, for one whose days have been devoted to investigations in the experimental laboratory to write a foreword on such a practical procedure as anæsthesia. Experience in the operating theatre alone was then admissible as a credential; and as far as the details of anæsthesia are concerned this is still true, and I should hesitate to express an opinion on these. But in this book the author is interested not only in the details of the methods but also in the general principles on which they are based, and here the experimental worker can help; in fact, this is his own domain.

Anæsthesia in its various aspects has been the subject of many writers, but has not hitherto been brought into close enough touch with the experimental sciences. In order to make this contact, a combination of practical and laboratory experience was required, and this has not been available. Dr. Levy has now shown how much the practice of anæsthesia in man is dependent on the principles of the basal sciences; how the same laws of physics hold in the ward and in the laboratory, and how necessary it is that the anæsthetist should recognize their bearing on his problems. His previous work on chloroform syncope has proved how advance in anæsthesia is to be made by experiments on animals. Without these it would have been impossible to ascertain the most frequent cause of death under chloroform —ventricular fibrillation—and to take measures to anticipate its occurrence.

This manual places the practice of anæsthesia on a new and firmer basis, and will be a boon to those

engaged in its practice. But not only the anæsthetist may benefit from it; it is a masterly analysis of the fundamental principles of the distribution of a drug in the tissues, which must interest a wider circle, for these principles obtain in large part when other drugs than chloroform are involved. We of the laboratory are furnished with a further point of contact with practice and with a further example of the importance of fundamental principles controlling active intervention in disease.

ARTHUR R. CUSHNY.

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Chloroform Anæsthesia

CHAPTER I.

The Physical Properties of Chloroform.

Chemical formula, $CHCl_3$.

Absolute chloroform has a specific gravity of 1·500 at 15° C., and a boiling point of between 61·1° C. and 61·2° C.

Commercial chloroform contains about 0·5 per cent. of alcohol, which is added in order to prevent decomposition, and has a sp.g. of from 1·490 to 1·495 at 15° C., and a boiling point between 60° C. and 62° C.

A "drop" of chloroform, according to Snow, weighs one-third of a grain (22 mg.), and consequently there are nine drops in two minims. Waller and Wells state that the drop varies according to the orifice from which it issues, but that from a stoppered bottle or "average" pipette the drop weighs 20 to 25 mg., which is the equivalent of 4 to 5 c.c. of vapour.

One gramme of chloroform when evaporated yields 197 c.c. of vapour at 15° C., or approximately 200 c.c.; one cubic centimetre of liquid chloroform weighs 1·5 grm. and yields therefore approximately 300 c.c. on evaporation at 15° C.

The vapour density of chloroform (compared with hydrogen) is 59·75, and it is approximately four times as heavy as air, the weight of 1 litre being 5·35 grm. at 0° C.

The latent heat of vaporization of chloroform is 61.

At its boiling point chloroform has a vapour tension equal to atmospheric pressure. At temperatures below boiling point vapour is evolved at lower tensions, and air is capable of taking up a proportion in the same ratio as the vapour tension bears to the atmospheric pressure.

Snow drew up a table of the maximum amounts of chloroform which the air will take up at different temperatures, based on direct estimations of the amount of liquid chloroform which could be vaporized in a given quantity of air at different temperatures; these estimations have been extensively quoted, but they are evidently somewhat rough, for they do not plot out in a smooth curve. Estimations of the vapour tension of chloroform at various temperatures have been made by Regnault, but ranging between the temperatures of 20° C. and 60° C. only.* It is possible, however, to plot off (with a negligible margin of error) a continuation of Regnault's pressure curve through lower temperatures by following the curve of similar water vapour pressures, so that data are obtained to calculate the percentages which saturate air throughout the range of temperatures included in Snow's observations. Parallel columns showing the percentage saturations derived from Snow's and Regnault's estimations are shown in the table below, from which it will be seen that Snow's estimations are for the most part too low.

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* Regnault's data are as follows :—

Temperature, centigrade	Vapour pressure, mm.
60°	755·4
55°	637·7
50°	535
45°	446
40°	369
35°	303·5
30°	247·5
25°	200·2
20°	160·5

Temperature, Fahrenheit	Saturation percentage of chloroform vapour in air at 760 mm. atmospheric pressure	
	Snow	Regnault
40°	6	10·0*
45°	7	11·0*
50°	8	13·0*
55°	10	15·0*
60°	12	17·0*
65°	15	19·5*
70°	19	22·1
75°	22	25·2
80°	26	28·4
85°	30	31·8
90°	35	35·5

* Approximate percentages from a continuation of Regnault's curve.

Purity of Commercial Chloroform.—Chloroform, as nowadays supplied specially for anæsthetic purposes, may be accepted as being free from impurities and can be employed without hesitation. It is therefore unnecessary to transcribe here the recognized tests for impurities in chloroform; they are described at length in Squire's "Companion to the British Pharmacopœia" of 1916. There is one important source of impurity, however, which it is necessary to avoid; exposure to air and sunlight leads to the formation of carbonyl chloride (phosgene) and possibly some other irritant vapours (Ramsay). For this reason chloroform should be stored in well stoppered bottles of tinted glass, and kept in a cool place. A small proportion of alcohol (about 0·5 per cent.) is added to commercial anæsthetic chloroform to retard this decomposition.

It may be noted here that chloroform vapour is decomposed by exposure to a flame into carbonyl chloride and hydrogen chloride, and in some cases in which chloroform has been administered in a confined space in the presence of a gas flame the results have been very serious for both the patient and attendants.

Commercial chloroform is prepared from three separate sources: (1) pure ethyl alcohol; (2) methylated alcohol (methylated spirit); (3) acetone.* In

* Chloroform prepared from acetone must not be confused with so-called "acetone chloroform" or "chloretone" which has a different chemical composition and properties.

regard to anæsthetic efficiency there is nothing to choose between these brands; chloroform prepared from acetone is, or was, the cheapest.

Wade and Finnemore, owing to a complaint made about the quality of the chloroform supplied at one time to Guy's Hospital, investigated the purity of chloroform made from ethylic alcohol and from acetone respectively. The chloroform supplied to the hospital was made from acetone, and it was alleged that its effect was slow and that it produced undue excitement. Wade and Finnemore found that acetone chloroform was remarkably pure, but that ethylic alcohol contained a minute trace, probably about 0·05 per cent. of ethyl chloride, which they suggested might be a beneficial adjunct in producing anæsthesia by stimulating the respiration. (This proportion of ethyl chloride works out at about 2 c.c. per Winchester quart of chloroform.) The writer subsequently compared different brands of chloroform from a clinical standpoint,* administering the anæsthetic by a similar drop method in each case and under conditions as similar as possible. The average time of induction with chloroform prepared from acetone, in twenty-five adult cases, was seven and a half minutes, and the average time for fifteen adults with ethylic chloroform was eight minutes. Holding the breath was noted rather less frequently under ethylic chloroform, but the figures given indicate fairly conclusively that the clinical distinction cannot be one of any significance. The complaint evidently originated from the use of a peculiar form of fabric mask which was at the time supplied in the hospital. It was very flat with much less in-curved margin than is usual in the ordinary form of Skinner's mask, and therefore it did not readily yield a sufficient supply of vapour (see Chap. XI). The circumstance is of interest and importance as illustrating how easily a confusion may arise between physiological and physical factors, and the large part

* Unpublished notes.

the latter play in the administration of volatile anæsthetics.

The Solubility of Chloroform in Water.—A volatile substance is dissolved in a liquid to saturation when its solution tension is equal to the vapour tension in a saturated atmosphere to which it is exposed. The determination of the total solubility of a volatile substance in a fluid is therefore a more delicate problem than that of a non-volatile substance, and it is not surprising that the estimations which are available differ considerably. Estimations of the solubility of chloroform in water are given in the following table according to various authorities named :—

	Temperature, Fahrenheit	By weight in gms.	By volume of vapour in c.c.
Squire's "Companion to the British Pharmacopœia"	at 60°	0·54 in 100	106 c.c. in 100 c.c.
Snow	„ 60°	0·52 „	102 „ „
Moore and Roaf	„ 55°	0·95 „	186 „ „
Gwathmey's "Anæsthetics"	„ 68°	0·82 „	161 „ „

Moore and Roaf's estimation was arrived at by two methods, gravimetric and chemical, which agreed in their result, and it may therefore be taken as probably the most accurate determination of total solubility in water.

The solution of a vapour in an inert fluid such as water is governed by the Dalton-Henry law; absorption is proportional to and directly varies with the "partial pressure" or "vapour tension" which is exerted, or, in other words, with the "percentage volume"* of the vapour in the atmosphere. Moore and Roaf have confirmed this law for chloroform; equal increments of chloroform are absorbed by water or saline solution

* The percentage of a vapour in air is generally expressed in terms of vapour volume; for example, a 3 per cent. atmosphere contains 3 c.c. of vapour in every 100 c.c. of mixture (i.e., 97 c.c. air + 3 c.c. vapour). The French percentage notation of grammes of volatilized liquid per 100 litres of air, as employed by Paul Bert, does not indicate the relative vapour pressures.

for equal increments of vapour pressure, so that the "curve" of solubility plots out as a straight line.

Solubility of Chloroform in Blood.—The solubility of chloroform in blood is a more complex matter, and it has not so far been determined in a satisfactory manner. Moore and Roaf find that blood alone when saturated takes up at 13° C. about 4 per cent. of chloroform by weight, and that whole blood, or a solution of hæmoglobin in water of equal strength to that contained in blood, takes up 6 per cent. at the same temperature; but both in blood and hæmoglobin solution a fine precipitate is formed long before the saturation point is reached, so that it is evident that the process is not one of simple solution. This fact is further emphasized by the observation that the solubilities of chloroform in serum and hæmoglobin solution do not obey the Dalton-Henry law, but plot out in curves, increments of dissolved chloroform being in excess of increments of vapour pressure. Moore and Roaf therefore deduce that chloroform forms a loose chemical combination, or "aggregation" with hæmoglobin and the proteids of serum, especially at the higher vapour pressures.

It is important to lay stress, however, on a point recognized by Moore and Roaf, but not sufficiently accentuated by them, that the solubilities in serum and hæmoglobin progress in a regular fashion up to 65 mm., and it is only at a pressure of 200 mm. that the curve becomes markedly apparent. Now a vapour pressure of 65 mm. is exerted by 8·5 per cent. of chloroform vapour in air, which is much higher than any concentration employed for anæsthetic purposes, so that we may conclude that serum and hæmoglobin, and presumably likewise blood, act to all intents and purposes as simple solvent agents in regard to chloroform vapour within the range of its lower or anæsthetizing percentages.

Moore and Roaf determined the solubility of chloroform in serum and hæmoglobin solution at 40° C. over a large range of vapour pressure, but they were unable

to perform the same experiments with whole blood; the solution of chloroform in whole blood at the lower vapour tensions is therefore a matter of conjecture, but possibly it approximates to that of its components.* Vernon Harcourt [1] performed a single estimation of the amount of chloroform taken up by blood when continuously exposed to a vapour of known pressure. He found that blood at 37° C. exposed to a 2·8 per cent. vapour, which has a partial pressure of 21·5 mm., dissolved 71 mg. per 100 c.c. According to Moore and Roaf's tables, the amount taken up by serum alone at 40° C. and at the same pressure is 92 mg. per 100 gm., and 84 mg. in the case of hæmoglobin solution. There may very well be a 20 per cent. error of deficiency in Harcourt's method, as he points out, and allowing this error, his estimation would approximately agree with Moore and Roaf's figure for serum alone. Much reliance cannot be placed on a single observation, but valuable information would be afforded by further investigations on the same lines.

It is very generally maintained that a larger proportion of chloroform is taken up by the corpuscles than by the serum of whole blood; seven to eight times as much according to Nicloux, and 97 per cent. as determined by Buckmaster and Gardner [3]. Byles, Harcourt and Horsley take the view that the red corpuscles when intact, and not laked as in Moore and Roaf's experiment, have a close affinity for a portion of the chloroform, so that it is not readily given up, but this affinity, in part at least, is dependent upon the length of time the chlorform is allowed to remain in contact with the corpuscles. It is perhaps doubtful whether such an affinity exists in the living body; in any case it seems evident that the conditions of the solubility of chloroform in blood form a field for further and more exact investigation.

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* See also Sherrington and Sowton's observations, p. 81.

The Estimation of Chloroform Vapour in Air.—The want of a ready means of estimating the percentage of chloroform vapour in air for long retarded the study of chloroform anæsthesia. This has in recent years been afforded in the densimetric method which was introduced by Waller and Geets; it is simple, and gives sufficiently exact results even in inexperienced hands. It has proved of much value in the estimation and control of the percentage vapour yielded by the various methods and apparatus in use for administration and experimental purposes, and hence has enlarged our knowledge of the action of chloroform upon man and animals to a very appreciable degree.* Another method, devised by Vernon Harcourt [2], is based upon the combustion of chloroform vapour by means of an incandescent platinum wire in the presence of steam; hydrogen chloride is formed, which is dissolved in water and titrated against dilute ammonia. This combustion method involves some chemical skill in its application, its performance is slow, and as it possesses no advantage over the densimetric method on the score of accuracy under ordinary conditions (Levy [8]), it is best reserved for special circumstances, e.g., for estimating chloroform in a moist atmosphere, as in expired air, or in the presence of other vapours.

The densimetric method consists, in effect, in ascertaining the difference in weight between a flask,† firstly filled with air, and secondly, filled with the chloroform and air mixture which is to be examined. This is performed in a single operation when once the flask has been counterpoised in a chemical balance by another similar flask. By making use of a flask of 250 c.c. capacity, the calculation of the percentage of the vapour

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* This method has been employed by Waller to estimate the chloroform in expired air, but it is doubtful whether sufficiently accurate results can be obtained in the presence of water vapour.

† Waller's densimetric flask may be conveniently modified by the substitution of hollow glass taps for the original stoppered inlet and outlet apertures.

by volume in 100 volumes of air is simplified, for then every centigramme excess weight represents 1 per cent. by volume, and similarly every milligramme represents 0·1 per cent. By making use of a flask of 260 c.c. capacity instead of 250 c.c. the correction for temperature is eliminated at 15° C., or about ordinary room temperature. A more accurate calculation may be made according to a formula given in the original paper.

Waller's "densimetric balance" automatically registers the approximate percentage of chloroform when a stream of chloroform-laden air is passed through it; it is more especially useful for demonstration purposes.

Estimation of Chloroform in Blood.—Various methods have been adopted for estimating the amount of chloroform in blood. Reference may be made to the Report of the Special Chloroform Committee of the British Medical Association and to the papers of Buckmaster and Gardner [3]. Nicloux's [1] method, however, appears to yield results as accurate as any, and is certainly the most simple in technique.

CHAPTER II.

Pharmacology and Toxicology.

(i) The Effect of Chloroform upon Tissue Parenchyma.

Numerous observations have been made upon animals which demonstrate fatty changes in the cell tissue of various organs, i.e., kidneys, intestines, heart, but more especially of the liver, as a result of the inhalation of chloroform. In the liver the fatty infiltration occurs mostly in the periphery of the lobules, the centres of which in some cases exhibit a definite necrosis. In the kidney the cells of the tubules exhibit some degree of fatty infiltration, generally slight. Fatty changes have also been described in the stomach. A detailed account of these parenchyma changes is given in a paper by Stiles and M'Donald.

It would appear that these changes are most marked following the prolonged or repeated administrations of chloroform. Whipple and Sperry make the interesting observations that the liver is normal at the end of an administration, and they consider that it becomes affected subsequently. Fatty degeneration of the liver has been found in man in most of the cases of death from delayed chloroform poisoning (see Chap. XIII), but necrosis of the centre of the lobule has only been noted in a small proportion of cases included under this category.

(ii) The Nerve Centres.

Chloroform depresses first the higher centres of the brain, thus abolishing sensibility. The motor centres are next affected, rendering the subject immobile and proof against sensori-motor reflexes. The centres

affecting circulation and respiration are the last to be seriously affected.

Chloroform, in common with most anæsthetic drugs, excites tissue function in the early stages of its administration.* The special senses and highest brain centres do not appear to share in the excitement; these are depressed very rapidly, so that the subject becomes largely unconscious with loss of conscious control of muscular action. The "stage of excitement" is manifested in a species of delirium, with talking and shouting and muscular movement or struggling; in poorly developed or asthenic persons excitement may be only slightly evident or even entirely suppressed, but in muscular and healthy persons it is generally more or less pronounced, and especially in alcoholic persons it may rise to a high pitch of intensity. The initial stimulation of the cerebral vaso-motor and respiratory centres, which will be referred to later, is apparently a manifestation of this general early excitement. There can be no question that the tendency to excitement is minimized when the strength of vapour administered is increased but very gradual stages and in a regular progression, but even under such conditions it is generally made evident in some degree.

The Vomiting Centre.—In protracted light anæsthesia the vomiting centre is excited to action, leading to "straining," or to the expulsion of gastric contents when present. This apparently is a direct action of the chloroform in the blood upon the centre, judging by analogy with the effect of ether, which may cause vomiting even when administered by the intravenous route. In full anæsthesia the vomiting centre does not come into action.

During recovery from anæsthesia the vomiting centre again becomes excitable, and vomiting is an almost invariable accompaniment of this stage. It is con-

* Hamburger's researches on phagocytosis incidentally afford a striking corroboration of this property of chloroform.

sidered by some that swallowed saliva, which contains a little dissolved chloroform, may act as a gastric irritant; certainly in the case of ether, which produces abundant salivation, the post anæsthetic vomiting does appear to be mitigated by measures adopted for draining the saliva from the mouth.

(*iii*) *Action on Nerve Fibres.*

Motor nerves appear to preserve their conducting function under full chloroform anæsthesia, but an ultra-anæsthetic strength of chloroform will abolish it. Waller [1] has shown that the direct action of a 4 per cent. vapour upon a segment of motor nerve exposed in a gas chamber practically abolishes its function. A 1 per cent. tension produces an appreciable reduction of conductivity, but it cannot be said whether this would obtain for a nerve lying intact in the body; the impression derived from physiological experiments is that nerves preserve their full excitability under chloroform anæsthesia of a surgical degree.

Clinical evidence shows that sensation may be depressed by chloroform even when the subject is not fully anæsthetized, as may be occasionally observed during partial recovery from the anæsthetic. It is probable that this is due to a persistence of the central nervous anæsthetic effect of chloroform, as there is no reason to suppose that the peripheral nerve apparatus is involved.

(*iv*) *Action on Skeletal Muscles.*

The contractility of voluntary muscle is unaffected by chloroform when present in the blood at an anæsthetizing tension; the strength of chloroform solution which effects a slight decrease in muscular contraction is sufficient to rapidly and permanently abolish the heart's beat.* The muscular relaxation under full chloroform anæsthesia is therefore entirely due to the

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* Sherrington and Sowton [2].

depression of the central nervous system, and consequent loss of muscular tone.

(*v*) *The Pupil.*

The pupil becomes small under anæsthesia of a distinctly light type; it is moderately dilated under full anæsthesia, and an excess of chloroform causes further dilatation. Hewitt gives the measurements of the pupil as 1 to $1\frac{1}{2}$ mm. in light anæsthesia, 2 to 3 mm. in deep anæsthesia, and $3\frac{1}{2}$ to $4\frac{1}{2}$ mm. in very profound anæsthesia. The cause of the contraction of the pupil caused by chloroform is not known.

The light reflex is abolished only in profound anæsthesia, but it should be noted that a condition of partial asphyxia appears to interfere with the elicitation of this reflex.

CHAPTER III.

Pharmacology and Toxicology. (*Continued.*)

(*vi*) *The Respiratory System.*

The Respiratory Passages.—A weak chloroform vapour is not unpleasant to inhale and is readily taken into the lungs, but as it approaches a 2 per cent. concentration its pungency causes it to be somewhat irritant to the respiratory tract, and it will be generally found that the sudden inhalation of a 2 per cent. vapour evokes a slightly choking sensation and a cough. The fully anæsthetized subject, however, can inhale chloroform of any concentration without reflex sequelæ.

The salivary secretion is excited by the inhalation of chloroform but not to an excessive degree, so that it is rare for any trouble to arise from this cause. An excessive mucous secretion from the trachea and bronchi is practically unknown under chloroform.

The Respiratory Movements.—The earliest effect of the administration of chloroform is a tendency to restraint of the respiration; there arises a sort of semi-conscious protest against the inhalation of the vapour, and not infrequently the breath is held either partially or completely for a brief period during induction. This restraint of respiration is probably the result of a sensory reflex through the vagus distribution to the respiratory surfaces of the lungs, and is comparable to the slowing of the respiration or total inhibition of it which is a result of the experimental excitation of the afferent vagus fibres.

The restraint vanishes as sensation becomes more affected, and then the respirations are found to be slightly accelerated, attaining in man a rate of from 20

to 30 per minute, and this is probably the result of an initial stimulation of the respiratory centre by the anæsthetic; should general excitement occur the respiratory centre is frequently excited to further action and the respiration rate may rise considerably higher.*

The ventilation of the lungs is normally the combined result of the movement of the thoracic walls and of the diaphragm, but, as the full effect of chloroform develops, the respiration frequently becomes largely diaphragmatic. Sometimes indeed the co-ordination between the chest muscles and the diaphragm is to all appearance lost, so that the action of the two mechanisms may appear to be antagonistic. The explanation of this puzzling condition is afforded in a paper by Hughlings Jackson and Collier. Paralysis of the intercostals commonly occurs under chloroform, more especially in deep anæsthesia; in such a case not only does the respiration become entirely diaphragmatic,† but the movements of the chest may become reversed, that is to say, the chest walls are sucked in during inspiration and recoil when the diaphragm is relaxed; sometimes, however, the upper ribs alone are raised by over-action of the scaleni muscles and the lower ribs everted whilst the middle part of the chest only falls in.‡

With further increase in the action of the chloroform the diaphragmatic movement is weakened in sequence to that of the intercostals, and consequently the total ventilation is considerably reduced.

Suppression of Respiration.—The weakening of the respiratory movements is the result of the action of the chloroform upon the respiratory centre. The final

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* The raising of the respiration rate from sensory reflexes in the course of operations is noted on p. 48.

† Previously noted by Paul Bert. The respiration again becomes costal on section of the phrenics.

‡ Under ether somewhat similar conditions are observed, but the intercostals never become entirely paralysed and some degree of elevation of the ribs persists, even thougb profoundly modified.

suppression of respiration from an overdose is largely dependent upon the same cause; but at this stage the heart has become greatly weakened by the chloroform, and the blood-pressure has generally fallen to a low level before the respirations finally cease. Leonard Hill [1] maintains that this fall of blood-pressure is actually the primary cause of respiratory arrest; no doubt it may be a contributory cause, but it is difficult to estimate the relative importance of the two factors involved. It may be accepted that respiration cannot be effectively carried on at a very low blood-pressure, but it is evident that Hill overstates his case, because respiratory arrest may be not infrequently observed, in physiological experiments, to occur before the blood-pressure has become seriously lowered, and even at times whilst it is rising. Further, it is a not uncommon clinical observation that the breathing stops whilst the radial pulse is still felt to be beating with considerable force. The primary cause of cessation of respiration is therefore paralysis of its centre.

The time which is taken to arrest the respiration by the administration of chloroform varies according to the concentration of the vapour. The rapidity of the passage of chloroform into the blood is proportional to the difference of vapour tension in the alveoli and the blood, so that an overdose is more rapidly effected by the inhalation of a stronger vapour.

Paul Bert's [1] observations upon the time taken to cause respiratory arrest in dogs by different percentages of chloroform vapour have been extensively quoted. They are as follows:—

Chloroform	Time of death
1·6 per cent.	4 hours
2·0 ,,	2 to 3 hours
2·4 ,,	Less than 2 hours
3·0 ,,	40 minutes
4·0 ,,	30 ,,
6·0 ,,	3 ,,

Note.—The percentages of chloroform were given in grammes of chloroform per 100 litres of air in Paul Bert's communication. His figures have been reduced here to terms of the volume of vapour per 100 volumes of air as is the usual notation in this country.

The time values given by Paul Bert are of course only generalizations. He says, "At the same dosage, dogs which appear to be under identical conditions die sometimes more quickly, sometimes more slowly than the average." That this is so is further exemplified in the following tabular summary of experiments undertaken by Levy and Rood,* in which percentages from 4 per cent. to 12 per cent. were administered to cats by means of an "ad plenum" method. A 2 per cent. vapour was given for two minutes in each case as a preliminary measure before administering the stronger vapour, in order to render the latter respirable. The net time taken by the strong vapour to stop the respiration is given in the table.

Percentage of chloroform		Time in minutes taken to stop the respiration
4·0	(kitten)	13
4·0	... ...	16¼
4·0	... ...	32
4·0	... ...	33
4·0	... ...	38½
4·0	... ...	42
4·0	... ...	43
7·0	... ...	8
7·0	... ...	10½
8·0	... ...	3
8·0	... ...	9
8 5	... ...	2¾
8·5	... ...	5½
9·5	... ...	3
12·0	... ...	7

The average time for 4 per cent. is thirty-one minutes, which is practically the same as Paul Bert's figure, but the actual range of variation is large.

The maximum percentage employed by Paul Bert was 6 per cent., and it is notable that higher percentages than this do not tend to stop the respirations any the more quickly. This is not remarkable considering the pungency of these vapours and the consequent restraint of the breathing, which becomes either very slow or else rapid and very shallow. The rate of lung ventila-

* Unpublished observations.

tion is an important subsidiary factor in deciding the time required for the introduction of an overdose (see Chap. VIII), as was in some cases evident; in other cases it appeared difficult to correlate the freedom of the breathing with the time of onset of respiratory failure, so that a strong impression was afforded that individual idiosyncrasy, or resistance to the effects of chloroform, plays a part in deciding the time taken.*

The following details of one experiment illustrate how the pulmonary ventilation generally diminishes towards the end, and that there is a definite warning of failing respiration long before the termination.

Time in minutes	Percentage of chloroform noted at intervals	Rate of respirations per minute	Description of respirations
0	2·0 per cent.	—	—
2	4·0 ,,	—	—
6	,, ,,	24	—
10	,, ,,	81	Shallow
11·30	,, ,,	96	,,
16	,, ,,	76	Heaving
24	,, ,,	64	—
25·30	3·8 per cent.	—	Shallow
28	,, ,,	48	Very shallow
31	3·5 per cent.	38	,, ,,
38	4·0 ,,	—	—
39	,, ,,	24	Very faint
40½	,, ,,	Final cessation of respiration	—

It is frequently difficult to determine exactly when the respiration finally ceases. Generally faint spasmodic efforts at inspiration may be noted at intervals of from

* The average effect of a given percentage of chloroform appears to be similar in many animals, but some parallel observations upon *rhesus* monkeys indicate a special susceptibility.

	Percentage of chloroform	Breathing ceases in
(1)	4·5%	7 minutes
(2)	4%	5 ,,
(3)	2% for 13 minutes, then 3% ...	19·45 minutes (total inhalation).

The times compare unfavourably with those given for dogs and cats, and there can be little doubt as to a special susceptibility of the *rhesus* monkey to chloroform poisoning.

5 seconds to 15 seconds in the final stage, and sometimes, following a temporary total cessation, regular respirations may be resumed for a brief interval. The decrease of the rate of respiration from its maximum is progressive in the foregoing experiment, but it is not always thus, for the respiratory rate may be maintained at a high rate, but the individual respirations becoming fainter and fainter until they die away in a few spasmotic attempts.

The Respiratory Gaseous Exchange.—It has been found that the intake of oxygen and the output of CO_2 are both progressively diminished (Paul Bert [3], Arloing) in chloroform anæsthesia, and it may further be taken as established by Buckmaster and Gardner [2] that the oxygen content of the blood is diminished and the carbon dioxide content is increased. Buckmaster and Gardner performed a series of analyses of the blood gases in cats under chloroform, and a summary of their results is given in the following table, the figures being all averages :—

Degree of anæsthetization	Average Volume in c.c. per 100 c.c. of Arterial Blood		
	CO_2	Oxygen	Nitrogen
Normal cats (no $CHCl_3$)	25·07	13·60	1·00
Reflexes just reappear	29·02	11·49	1·33
Reflexes just disappear	29·57	7·78	2·15
Second stage of anæsthesia (full anæsthesia)	36·00	8·14	1·49

Both these sets of observations are conformable with a diminished rate of pulmonary ventilation during anæsthesia, due to depression of the respiratory centre. Buckmaster and Gardner [1], however, maintain that the diminished oxygen content of the blood is not due to diminished ventilation, but to a diminished power of hæmoglobin to take up oxygen when affected by chloroform. It is difficult to agree with Buckmaster and

Gardner that their tables and diagrams disprove a falling off in the ventilation; on the other hand, they may be interpreted as showing distinctly that the ventilation generally falls to a lower level under chloroform, although the results are somewhat irregular.* Further, Moore and Roaf show by direct observation that chloroform at anæsthetizing tensions does not depress the oxygen absorbing power of hæmoglobin, and an experiment performed by Tissot directly negatives this assumption.

Tissot administered chloroform to a dog, and at the same time maintained a full degree of ventilation by means of artificial respiration. He analysed a sample of blood at the moment the heart stopped beating from an overdosage of chloroform, and found the blood then held a full content of oxygen; this experiment appears to demonstrate conclusively the undiminished capacity of hæmoglobin to take up oxygen even when containing a maximum amount of chloroform, and leads us to conclude that the changes in the blood gases and the gaseous exchange are simply determined by the diminished pulmonary ventilation under full chloroform anæsthesia. Buckmaster and Gardner's results certainly show a seriously reduced oxygen content of the blood in chloroform narcosis, whatever the cause may be; possibly a reduced blood-pressure may conduce to the result, and this is a factor which has not been taken into account. At the same time it should be noted that the average normal oxygen capacity in cats is a very low one (in man it is about 20 c.c. per 100 c.c. of blood), and it may be inferred, therefore, that the oxygen content in man is not reduced in chloroform anæsthesia to the same low level that it is in cats.

* Unfortunately the authors have not been able to provide a standard of normal respiration, without which it is difficult to interpret the results.

CHAPTER IV.

Pharmacology and Toxicology. (*Continued.*)

(*vii*) *The Action of Chloroform upon the Circulation.*

The Rate and Rhythm of the Heart-beat.—R. Gill states, as the result of a large number of clinical observations, that the average pulse-rate is 73 in males and 75 in females during the first five minutes of the anæsthetic action of chloroform. Later, during full anæsthesia, the rate of the pulse is not greatly affected as a rule by the uncomplicated action of the chloroform, that is, considered apart from such alterations as are due to reflexes induced by surgical procedures, which generally tend to accelerate it. In cats a slight slowing is frequently observed, and in man likewise the tendency is similar.

I have frequently observed the abrupt administration of a strong or moderately strong vapour to a conscious animal or one already partially under the influence of chloroform, to produce an immediate slowing of the heart-beat; thus the rate was in one instance observed to fall from 210 to 150 on the sudden administration of 3·5 per cent. chloroform to a cat, and in several other instances an accelerated pulse was similarly restrained to about the normal rate (i.e., 120). This is no doubt a vagal effect, a reflex arising from the stimulation of the nasal sensory nerve endings by the pungency of the vapour.*

In animals under very deep anæsthesia the heart-beat is as a rule materially slowed, and this slowing may or may not be associated with a form of heart block in

* A striking example of such a reflex is obtained by puffing tobacco smoke on to the nostrils of a rabbit.

which the auricular and ventricular beats are completely dissociated. The slowing, however, is not due to the block, because the auricular contractions are slowed to approximately the same rate as the ventricles; further, the condition is not generally persistent, and the heart reverts to a normal sequential beat, but still at the same slowed rate.* I have observed dissociation in electro-cardiographic records as the result of the continued administration of a high percentage of chloroform (4 per cent. or over) to cats, and the condition was associated with a fall of pulse-rate in one case from 208 to 160 per minute, in another from 214 to 113, so that the slowing is very notable. Hecht and Nobel, who were the first to record heart block under chloroform, have also recorded conditions of 2 : 1 and 4 : 1 block. There is no evidence that this block may lead to cardiac stoppage or any serious consequences, but it is probable that the slow rates sometimes observed in man, such as 40 to 60 beats per minute are, *when the patient is deeply anæsthetized,* due to this cause.†

In dogs an extreme slowing of the pulse, down to 30 beats per minute, may sometimes be observed in the final stages of overdose, and this is without doubt conditioned by vagal action, for the rate is accelerated on section of the vagi.

I have on rare occasions found in cats an irregularity of the pulse due to the incidence of ventricular extra-systoles during deep narcosis, but when these occur the records tend to show they are frequently conditioned by a previous accidental respiratory obstruction, and the mechanism of their origin will therefore appear later (p. 31). In a few cases, however, there was no direct

* Unpublished notes.

† Lewis and Matheson have shown that heart block occurs in a late stage of asphyxia and the question arises how far does an asphyxial factor enter into the causation of the chloroform block ; I have, however, observed this condition some time before the respiration has become embarrassed, and although the oxygen content of the blood may be somewhat diminished, yet the deprivation would not appear sufficiently advanced to produce the block in itself and I am inclined to regard it as a block of toxic (chloroform) origin.

evidence of an asphyxial complication and the origin of such irregular beats in deep anæsthesia must remain open to speculation.

A sudden drop in the pulse-rate to about half the previous rate is sometimes observed under anæsthesia which is light or certainly not abnormally deep; this is always due to the incidence of alternate dropped beats, or "pulsus bigeminus," the alternate premature beats being too weak to be conveyed to the wrist. This leads to the consideration of the important subject of the "irritability" of the heart, or rather of the ventricles of the heart, under chloroform, the term "irritability" being employed to denote a tendency to the occurrence of premature beats or extrasystoles.

Cardiac Irritability under Chloroform.—The ventricles of the mammalian heart are in an irritable condition when affected by chloroform. This irritability is most marked when they are lightly affected by chloroform, and is progressively diminished under conditions of deepening anæsthesia. (Levy and Lewis.)

Although thus made irritable, extrasystoles of ventricular origin are not evoked by the chloroform *per se*, but an exciting cause must be superadded (Levy [1]); such exciting causes are:—

(1) Conditions which stimulate the ventricles.

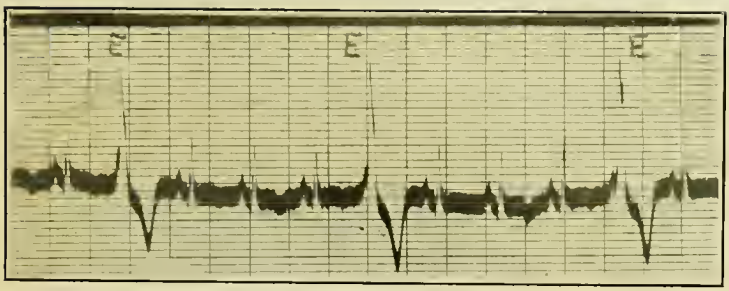
(2) Conditions which remove or reduce depressing influences, and are thus the equivalent of a stimulation.

Ventricular extrasystoles under chloroform have been conveniently studied in the heart of the cat, which is particularly liable to this affection. In the heart of man these are no doubt less frequent in occurrence, but may often be observed under appropriate circumstances by careful observation.* C. D. Edwards found that the pulse became irregular in no less than eleven out of twenty-five cases of chloroform administration which he had under observation, but the form of irregularity is not stated.

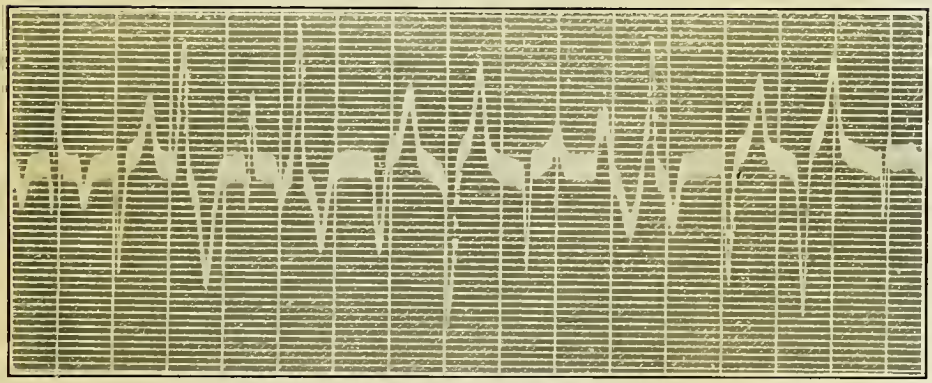
* Electro-cardiographic observation of the heart-beat of man under chloroform is wanting at present and is evidently desirable.

Ventricular extrasystoles under chloroform present a great diversity both in regard to their nature and sequence. They may be observed as isolated dropped beats, or in a regularly recurring sequence, such as the "bigeminal" or "trigeminal" beat, every alternate or third beat being an extrasystole (fig. 1, A); in other cases extrasystoles arising from different points in the muscle walls of the ventricle occur at irregular intervals, recorded as a complex pulse tracing difficult to analyse. In the most intense exhibition of extrasystoles the sequence is a rapid succession which in the cat may attain the rate of 300 per minute (the normal heart-beat having a rate of about 120 per minute). In such a condition every beat is an extrasystole, there being no longer any normal beats to be found; it is technically described as a "multiple extrasystolic tachycardia" (fig. 1, B and fig. 5). The serious interest which this latter condition possesses for the anæsthetist is that it is a condition of potential fibrillation, for it is liable to pass suddenly, by an acute transition, into the condition known as ventricular fibrillation, with a consequent and frequently permanent cessation of the circulation.* The onset of ventricular fibrillation is marked by a precipitate fall of blood-pressure, for the preceding irregular tachycardia is a sequence of co-ordinate (although abnormal) heart-beats, which sustain the blood-pressure, but with the onset of fibrillation the ventricles do not beat at all, and become entirely inert in respect of their capacity of emptying their cavities (fig. 2).

* The intrinsic mechanism of ventricular fibrillation has been discussed in papers by Mines, Garrey and Levy [2]. The cognate condition of auricular fibrillation has recently been dealt with by Lewis and his collaborators in a long series of papers. Ventricular fibrillation is readily identified in electrocardiograms, being characterized by rapid fluctuations of electric potential, the rate in the cat being from 500 to 600 per minute. The heart of man is a slower acting organ than that of the cat and the fibrillation rate is slower, as appears from an electrocardiogram obtained by Robinson and Bredeck, in which it is 280 per minute. It is probable that the rate of the preceding multiple tachycardia is likewise slower in man. The same observers show a curve of this condition in man (following the injection of strophauthin) which has a rate of 120 per minute, but further evidence is required on this point.



(A)



(B)

FIG. 1.—Electrocardiograms of abnormal ventricular beats under light chloroform anæsthesia. Cat. The vertical lines indicate intervals of $\frac{1}{5}$ of a second.

(A) Every fourth beat is an extrasystole (E). The intermediate beats are normal.

(B) Every beat is an extrasystole, and each is of a different type.

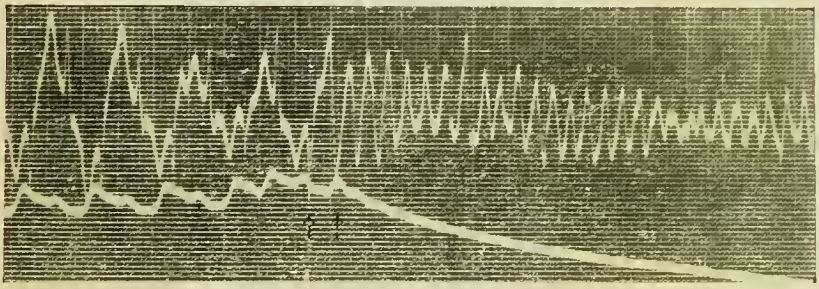


FIG. 2.—Combined electrocardiogram and blood-pressure record from a cat under chloroform (Hürtle membrane manometer). In the first part of the diagram there is shown a rapid succession of extrasystoles which terminate abruptly in ventricular fibrillation. The blood-pressure commences to fall with the onset of fibrillation. The extrasystoles in this instance arise alternately from the right and left ventricles; their rate is about 300 per minute.

We may now consider in detail the various forms of stimulation which are known to lead to the manifestation of ventricular extrasystoles under chloroform, but first it must be repeated that light anæsthesia is an essential condition, and that under deep anæsthesia they are far more difficult to evoke and are generally suppressed, and further, that under deep anæsthesia they have *never been observed to progress to the fatal condition of ventricular fibrillation.*

First we may consider the important condition of "passive" stimulation, or in other words, stimulation by removal of a depressing influence. This is strikingly exemplified experimentally by cutting the vagal trunks in the neck of a cat; the normal result is that the heart beats more quickly and more strongly, or in other words is stimulated, and as a consequence, under light chloroform anæsthesia, the heart becomes extremely irregular; it may pause momentarily at intervals owing to short phases of ventricular fibrillations, and it may ultimately fail permanently from this cause. This experiment probably has no clinical parallel, but the effect of reducing the supply of chloroform to a heart already well under its influence, is analagous. As the heart recovers from the effect of chloroform its action is augmented,* and ventricular extrasystoles make their appearance. At first these may be only evidenced by occasional dropped beats, later we may note a regular sequence of them in the form of trigeminæ or bigeminæ, and these may pass into a more complicated sequence, terminating on occasion, and on occasion only, in ventricular fibrillation. This effect of reducing the supply of anæsthetic is readily demonstrated in the cat; probably it is of more rare occurrence in the human subject. Even in the cat, if the heart has been subjected for some time to a full dosage of chloroform, then the irregularities may be only slightly manifested, or indeed entirely suppressed.

* The analogy is not complete for the augmentation is in this case mainly in *force*, and the rate is only slightly accelerated.

Now let us turn to the condition of a direct stimulation of the heart. One of the most powerful of cardiac stimulants is adrenalin, which excites the myoneural junctions of the cardiac sympathetic nerves. The injection of a small quantity, 0·065 mg. (= 1 minim of a 1 in 1,000 solution of adrenalin), into the vein of a cat which is only lightly anæsthetized and is exhibiting an active corneal reflex, produces an intense ventricular tachycardia, which almost invariably terminates in ventricular fibrillation in from 15 to 20 seconds.* In a cat fully anæsthetized by chloroform the irregularities may or may not be produced, generally not, but even if they do occur ventricular fibrillation *never* follows under such a condition (fig. 3).

This experiment has a clinical counterpart when adrenalin is absorbed following an injection of it for surgical purposes (for illustrative cases see p. 99 and also Levy [3]), but it likewise has a physiological counterpart, for the adrenal glands may be excited to secrete sufficient adrenalin to cause ventricular irregularities and even death by ventricular fibrillation under chloroform. The secretion of the suprarenal gland is controlled by the splanchnic nerve, and any physiological sympathetic impulse, it may be arising from an emotion such as excitement or as a reflex from sensory stimulation, will cause an excess of adrenalin to pass into the blood and produce a cardiac effect in light anæsthesia; deep anæsthesia will naturally suppress both these influences.

It was at first thought that the vaso-constrictor effect of adrenalin might have a causal relation to the ventricular irregularities, from throwing a strain upon the heart, but this was subsequently proved not to be the case.† The function of adrenalin which excites the extrasystoles is stimulation of the ventricles through the

* This experiment is more generally successful when the anæsthesia is very gradually reduced following a full, but not deep, preliminary narcosis. Dogs appear to be equally susceptible to this reaction.

† Levy [4].

sympathetic (accelerator) nerve endings. The result of directly exciting the sympathetic nerve supply of the heart, that is, the stellate ganglion or the accelerator nerve, by applying a faradic current, is similar to that of the injection of adrenalin, with the difference only that the irregularities are not produced with quite such

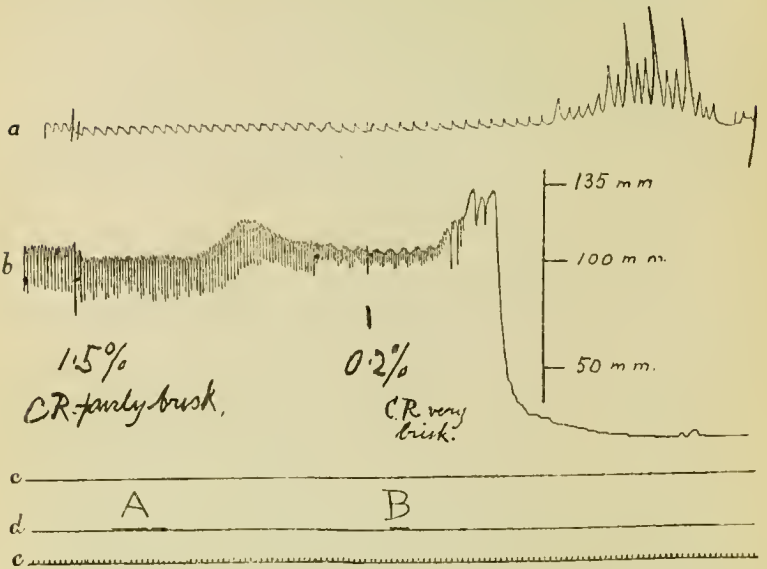


FIG. 3.—Respirations and blood-pressure records showing the reaction to adrenalin in a cat under chloroform.

a, Respiration. *b*, Blood-pressure (mercury manometer). *c*, Level of zero-pressure. *d*, Signal line. *e*, Time, indicated in seconds.

A, Intravenous injection of half a minim of 1 in 1,000 adrenalin solution under 1·5 per cent. chloroform. The blood-pressure rises, but the beat remains regular. B, A similar injection under 0·2 per cent. chloroform. The beat becomes rapid and irregular and finally ceases abruptly.

Following the cardiac collapse the respirations are first greatly exaggerated and they cease entirely.

certainty and intensity, and a fatal conclusion occurs in only about two-thirds of such experiments (fig. 4). The effect of light and deep anæsthesia in this connection is precisely the same as with adrenalin.

A direct action of the cardiac accelerator centre is manifested in the emotional condition which accom-

panies the struggling or "excitement" which may occur in the early stages of the induction of anæsthesia, and which is a frequent precursor of ventricular

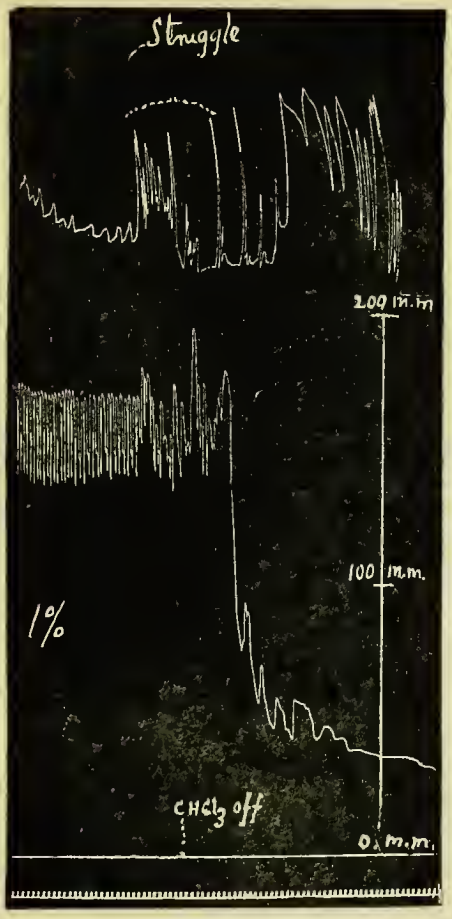


FIG. 4.—Ventricular fibrillation initiated during a fit of struggling in a cat under light chloroform anæsthesia. Upper record, respiratory. Lower record blood-pressure, mercury manometer. Time marked in seconds.

The period of struggling is indicated by the irregular respiration record within the dotted bracket. The cardiac collapse is followed by intense dyspnœic gasps. The heart was inspected immediately on the cessation of respiration, and the ventricles were seen to be fibrillating vigorously.

(The declination on the left of the respiratory record is accidental).

fibrillation (fig. 5). Powerful sensory impressions such as would normally create the sensation of pain send a reflex impulse through the cardiac sympathetics, and the incidence of ventricular extrasystoles from electric stimulation of sensory nerves may be demonstrated readily enough; the climax of ventricular fibrillation is, however, a relatively rare event in this connection.* For the success of this experiment carefully regulated light anæsthesia is essential not only on account of the direct action of full anæsthesia on the heart, but likewise because it damps or cuts out entirely the reflex mechanism.

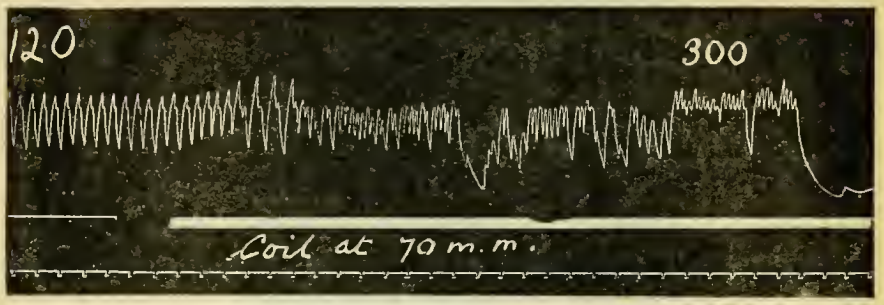


FIG. 5,—Excitation of the cardiac accelerator nerves with a faradic current, in a cat under 0·5 per cent. chloroform. The heart-beat becomes highly irregular and interrupted by short pauses, and finally fails abruptly and permanently in ventricular fibrillation. The figures above the curve indicate rates of heart-beat. The signal mark indicates the duration of the faradic excitation. Hürtle membrane manometer. Time marked in seconds. (Natural size.)

An important form of sympathetic reflex arises from the mucous membrane of the upper air passages.† Probably any powerful irritant will serve the purpose, but chloroform vapour itself in a concentration of about

* In a series of forty experiments in which the central end of a cut sciatic nerve was stimulated the irregularities terminated in ventricular fibrillation on six occasions; the fibrillation was permanent and fatal in two only. Sensory impressions arising in the splanchnics area are, however, more potent.

† A *vagus* reflex likewise arising from the nasal mucous membrane has been referred to (p. 21.) but this has little potency when the heart is already irregular. The accelerator reflex may be demonstrated with greater success after the vagi have been paralysed with atropin. (Levy [5], p. 7.)

2 per cent. or over is sufficiently pungent to evoke cardiac irregularities, if suddenly applied after an interval during which no vapour has been given. The re-application of chloroform is particularly potent in adding an extra stimulation which is sufficient to evoke the final catastrophe of ventricular fibrillation when the heart has already been made irregular from any of the other causes which have been mentioned, and the reaction may be of very rapid, almost instantaneous nature.

Extreme deprivation of oxygen is also an exciting cause of ventricular irregularities under chloroform, for the whole of the sympathetic system is excited, the heart being directly stimulated through the accelerator nerves, and indirectly from an increased suprarenal secretion (von Anrep). It is to be observed, however, that asphyxia depresses the heart, and so is to a large extent a deterrent to actual fibrillation of the ventricles, although this may occur as an exceedingly rare event.* Although this is the case the extrasystoles may persist and be accentuated on the reversion to normal ventilation with air without chloroform, and therefore it is possible the irregularities may pass into fibrillation during recovery from asphyxia.

All cardiac depressants tend to prevent fibrillation through their action upon the heart muscle.† Increased vagus tone likewise acts in this way and tends to diminish the onset of extrasystoles, so that vagal action is protective against these dangerous irregularities. The cardiac depressant which is the most powerful antagonist to the irritable phenomena of the ventricle is *chloroform itself in full doses,* and this fact should constantly be kept in mind.

Recovery from Ventricular Fibrillation.—Ventricular fibrillation is not necessarily a fatal event, for the heart

* Even such a powerful and certain fibrillating agent as adrenalin only produced its maximum effect once in seven experiments upon cats asphyxiated under chloroform.

† Levy [4].

may recover spontaneously. There is a tendency to recovery in all animals, but this varies greatly in degree; in the dog recovery is rare, in the cat not infrequent, and in the rat almost the rule. The period within which spontaneous recovery can occur is, however, strictly limited, because the heart muscle becomes asphyxiated from cessation of the circulation. I have never observed spontaneous recovery to occur later than one minute and twenty seconds from the onset of fibrillation in the cat's heart; recovery may, however, be fostered with uniform success in this animal by massaging the heart under artificial respiration and so restoring an effective circulation (Levy [15 and 16]).

Spontaneous recovery may not entail permanent survival, for the ventricles may be irregular on recovery and a second syncope may occur, which is generally final, although a second recovery has been observed on rare occasions.

That spontaneous recovery from ventricular fibrillation may occur in the heart of man is proved by the electro-cardiographic record obtained by Robinson and Bredeck; this subject, together with that of cardiac massage, is dealt with in detail in Chapter X.

The Force of the Heart-beat.—The source of the fall of blood-pressure which is caused by chloroform was at one time a much debated subject; thus the Hyderabad Commission contended it was of vaso-dilator origin, and that the force of the heart-beat was only affected at a late stage of chloroform poisoning mainly as a result of asphyxia brought about by failing respiration.

The more recent investigations into the action of chloroform upon the blood-vessels are discussed later, and they do not support the view that a general dilatation occurs. On the other hand, it is now generally agreed that the force of the heart-beat is profoundly weakened by chloroform and that the fall of blood-pressure is mainly due to this fact.

The depression of the heart by chloroform has been

demonstrated by many physiologists, but we need refer here only to the more recent work of Sherrington and Sowton [1], which conclusively demonstrates the depressing effect of chloroform upon mammalian heart muscle by a number of precise experiments which set at rest all doubt upon the subject. The method they employed was perfusion of the isolated mammalian heart through its coronary vessels, and briefly stated the experiments show :—

(1) That the heart is weakened progressively as the strength of the chloroform in the perfusion fluid is increased.

(2) That the effect is rapidly made evident, and is maintained so long as the perfusion continues, and

(3) That it rapidly disappears on reverting to chloroform-free fluid.

(4) If, however, chloroform is perfused in sufficient strength, the beat becomes after a little while permanently abolished and does not recover.*

Perfusion with chloroform in oxygenated blood reduces the ventricular beat on an average as in the following table :—

Chloroform in 100 c.c. of blood	Percentage reduction of ventricular beat
0·033 grm.	4
0·050 ,, ...	35
0·075 ,, ...	75
0·100 ,, ...	95, with permanent damage

It is important to note that so long as the vapour tension is constant, the force of the heart-beat likewise remains constant, it does not diminish further even after a long time, and if anything tends to improve a little; that is to say, the depressive effect is not cumulative.

At the same time that the heart is weakened in its force of contraction it dilates, and this dilatation is seen in plethysmographic curves to occur with remarkable rapidity, and to vary in degree according to the per-

* The heart is never in practice overdosed to this extent for the respiration fails first, so cutting off the supply of chloroform. Even by adopting extreme experimental measures with an inhaled 4 per cent. vapour I have failed to abolish the heart-beat beyond the possibility of recovery.

centage of vapour with which the lungs are ventilated. Hill [2] points out that the force required to empty the ventricles increases as the cube of the radius, and that the extra mechanical strain thus thrown upon a heart already weakened in physiological power may result in a serious disability. It appears doubtful, however, whether such dilatation of the heart occurs to any serious degree under ordinary circumstances. In the plethysmograph experiment the heart is stripped of its pericardium, which must under clinical conditions afford it support and limit its expansion; the dilatation under normal physiological conditions in all probability is largely potential only, so that the heart beats with a weakened force of contraction and probably with little other disability.

The Failure of the Heart in Overdosage.—For many years it was a debatable point whether the heart or respirations stopped first in fatalities under chloroform. This inquiry can be restricted by the question: "Which fails first in overdosage?" and the Hyderabad Commission in its two reports showed by numerous experiments that the heart's action only became "dangerously affected or stopped" subsequently to the cessation of the respiration as a result of overdosage with chloroform; in 571 overdosed animals (mostly dogs) the respiration ceased before the heart in every case. The arterial pulse always disappeared before the cessation of the heart-beat, as was demonstrated by the movement of a needle thrust into the heart through the chest wall, and confirmed by direct inspection. The following figures are taken from the First Report:—

Interval between the complete arrest of respiration and disappearance of the heart-beat:—

Maximum time			Minimum time
13 minutes 40 seconds	...	...	45 seconds

Interval between the complete arrest of the respiration and disappearance of the arterial pulse:—

Maximum time			Minimum time
7 minutes 52 seconds	...	...	5 seconds

The contention of the Second Hyderabad Commission that chloroform has little direct action upon the heart, and that its failure is mainly due to asphyxia, we now know to be erroneous, but, on the other hand, we cannot attribute the heart's failure entirely to depression by chloroform; the supply of chloroform is cut off by the suspension of the respiration whilst an arterial pulse is still being propagated, and as the action of chloroform is not progressive, there is no reason why the heart should fail still further from this cause. In my experience partial asphyxia from failing respiration depresses the heart considerably under chloroform, and I believe the weak action of the heart at the moment of respiratory arrest is in part due to this cause; the final extinction of the heart's beat can only be attributed to total asphyxia.

It is further important to remark that loss of the pulse in the systemic arteries does not necessarily imply cessation of the pulmonary circulation, in which the peripheral resistance is lower, being about one-sixth of that of the systemic resistance. There is good reason to believe likewise, that a measure of circulation is maintained in the coronary vessels at a very low pressure; this circulation is fostered by the movements of the heart, and also probably by the tendency of the coronary arteries to dilate in asphyxial conditions.

The foregoing facts will be taken into consideration in examining the mechanism of artificial respiration when employed as a restorative measure.

Cardiac Inhibition under Chloroform.—The cardio-inhibitory centre has been accredited by several observers with playing an important part in the production of syncope under chloroform, but with the exception of Embley's work little experimental evidence has been advanced in support of this contention. Embley claims that during the earliest stages of the administration this centre is directly excited by chloroform, causing a pronounced slowing or else the actual arrest of the heart-beat, from which there may be no

recovery, and that the effect is not observed after once anæsthesia has been well established. Embley's experiments were performed on dogs, and in order to observe the effect of the chloroform from the very commencement of the administration the animals were given a large dose of morphia, under the influence of which the preliminary operation of connecting a cannula with a carotid artery was performed, before the chloroform was administered. The amount of morphia employed varied from 0·25 gm. (about 4 gr.) up to 0·5 gm. (7·5 gr.) according to the weight of the animal.

Briefly, Embley's conclusions were as follows :—

In 54 out of 124 experiments, vagus inhibition embarrassed the circulation to a more or less dangerous extent, and in 33 was the immediate cause of death.

With a 2·2 per cent. vapour cardiac inhibition occurred in one case after a lapse of 4 minutes 50 seconds, with a 3 per cent. in 3 minutes 10 seconds, with a 4 per cent. in 2 minutes 25 seconds. With chloroform under 3 per cent. strength the heart always recovered from the inhibition, but at 3 per cent. and over the inhibition was frequently permanent and fatal.

Such results as the foregoing have not been observed in non-morphinized animals. Embley himself performed a series of experiments without morphia for purposes of control and obtained entirely different results. Out of twelve experiments, eleven showed nothing that can be surely attributed to vagal inhibition. In the remaining single case the heart was inhibited 3 minutes 35 seconds from the commencement of the administration, when the blood-pressure had already fallen to 25 mm. Hg. The amount of chloroform was described as " considerable " ; judging from the fact that the pressure was reduced to 25 mm. in the time given, the percentage must have been over 5 per cent. and was possibly much higher. This single experiment does no more than show that an inhibition may possibly occur, as a result of overdosing an animal with a vapour higher

than that employed in clinical usage, and sufficiently strong to reduce the blood-pressure with great rapidity.*

It appears evident that the large doses of morphia employed played an important part in the production of the inhibition phenomena in the early stages of the chloroform administration, and as it is upon these morphia experiments that Embley bases his theory of cardiac syncope and death through vagal action, this cannot be regarded as a satisfactory explanation of sudden death.† Furthermore, it remains to be demonstrated that even in these morphia experiments vagal inhibition is ever persistent and fatal when artificial respiration with pure air is promptly applied.

Reflex vagal inhibition of the heart may be most readily induced experimentally by the electric excitation of the central end of the cut recurrent laryngeal nerve, or of the main vagal trunk, or again, it is stated, of the sensory branches of the fifth nerve; such excitations will produce a slowing of the heart which may be extreme, accompanied by a fall of blood-pressure.‡ The heart always escapes from the vagal reflex, however long the stimulus be applied, and such a condition as permanent arrest of the heart through a vagal reflex is unknown in experimental physiology.

It has been held without any real proof, that in the early stages of chloroform administration the vagus reflex is exalted, but however this may be, it is certain that the reflex is diminished with progressive narcosis, like other reflexes. Bearing in mind that the vagus centre is excited by asphyxia, A. G. Levy [6] investi-

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* Schafer and Scharlieb's observations appear to confirm this late vagal effect of massive doses of chloroform. They say the heart always recovers under artificial respiration. They do not give full experimental details, and omit any reference to the use of morphia as an adjunct to the chloroform. On the other hand the experiments of the Hyderabad Commission already referred to (p. 34) are directly opposed to Embley's theory.

† It is notable that Embley's theory covers only the induction period of anæsthesia and offers no explanation of death at later stages.

‡ Reid Hunt maintains that a vagus reflex may be obtained from any sensory trunk if the stimulation be sufficiently strong, but the effect is quite small.

gated the influence of asphyxia upon vagal reflexes in animals under chloroform. His results showed that the reflex is obscured or suppressed by complete asphyxia,* but it was frequently somewhat exaggerated during partial asphyxia. In no case throughout a long series of experiments with and without asphyxia was there even a suggestion that permanent arrest of the heart was possible through a reflex mechanism. The results did not differ materially from those obtained in similar experiments under ether anæsthesia.

Theories regarding reflex cardiac inhibition have been advanced by Dastre and by Morat and Doyen, and have been extensively quoted to explain cases of sudden cardiac syncope occurring during operations under chloroform; this is, however, simply an explanation *faute de mieux,* for it has no experimental support.†

No doubt reflex vagal effects may be observed under chloroform in the form of a slowing up of the pulse, or even possibly as a temporary syncope (Richet [2]). How far such vagal reflexes apparent during operations under chloroform? This is a question not easily answered. A slowing of the pulse is said to be sometimes observed during operations in sensitive areas, but beyond saying that we should certainly expect such reflexes during laryngeal operations and operations upon the lungs,‡ we must leave the question to be settled by further careful clinical observation.

Ordinary fainting attacks such as may occur at the sight of blood, are no doubt emotional and vagal in origin (Lewis and Cotton), and can hardly occur in a state of unconsciousness.

The Action of Chloroform upon Blood-vessels.—Importance has been attached to a presumed depressing action

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* This observation is in agreement with that made by François-Franck.

† MacWilliam [1] considers that the theory of permanent arrest of the heart by reflex vagal inhibition may be set aside as devoid of foundation.

‡ Cardiac inhibition arising reflexly from both these sources of origin is accompanied by partial or complete arrest of respiration which may help to identify the reaction.

of chloroform upon the vasomotor centres leading to vaso-dilatation. MacWilliam [2], L. Hill [1], the Hyderabad Commission, Alexander Wilson and others have advanced this theory, and Wilson has attributed sudden death under chloroform to this cause. There is little experimental evidence, however, in support of this view. Gaskell and Shore deny that any vaso-dilatation occurs as a result of central nervous action, and they have further shown that at least the primary action of chloroform is in an opposite direction, and that it causes a constriction of the blood-vessels by exciting the vasomotor centres in the brain, causing a rise of blood-pressure, which antagonizes the fall due to central cardiac depression. Embley confirmed this fact, and found that a central vasomotor effect of this nature could be elicited even after 103 minutes of sound surgical anæsthesia.

I have myself made a considerable number of observations which tend to confirm this occurrence.* As an example, 2 per cent. chloroform caused in one instance a rise of blood-pressure from 144 (normal) to 198 mm. (the animal meanwhile remaining perfectly motionless), the pressure still being 174 mm. after three and a half minutes' administration; such a continued effect is not however always maintained, and in some cases the pressure fell to normal within the space of one minute.†

How far this active vaso-constrictor action is continued throughout narcosis it is difficult to say, but it appears probable that it counteracts for some time the tendency to a fall of pressure from cardiac weakness, if not permanently, for it is a question whether the blood-pressure could otherwise be so well maintained as it is in animals, even when the heart-beat is accelerated.

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* These experiments were performed on animals prepared for the registration of the blood-pressure by a painless method but without the introduction of any drug into the circulation, so that an uncomplicated result was obtained on the exhibition of chloroform. (Levy [1], p. 322).

† The fact that the rise is frequently sustained lends support to the view that it is caused by chloroform in the blood and not by a sensory reflex.

The condition of the blood-vessels under chloroform is not, however, as simple as stated above, for Embley has shown that chloroform administered in clinical concentrations causes a local dilatation of the vessels of the abdominal organs (intestines, spleen, kidneys) from a direct action of the chloroform upon the plain muscles of these vessels.* The dilatation is probably not very pronounced under ordinary anæsthetizing vapour tensions, and may be kept in check by the constrictor influence already dealt with, but it possibly exerts an uncomplicated and notable effect in the deeper stages of anæsthesia.

L. Hill's contention that chloroform abolishes the vaso-constrictor mechanism is in part based upon the fall of pressure observed upon tilting an animal into a vertical position when under chloroform; this result would appear to be explained by Embley's observations, and does not necessarily entail a general vascular dilatation.†

The reaction of the blood-vessels of the skeletal muscles to the perfusion of a solution of chloroform in Ringer's solution has been considered by Schäfer and Scharlieb, who noted vaso-constriction from the action of the chloroform upon the plain muscles of the vessels, but only to a slight extent, causing about 10 per cent. reduction of flow; similar experiments were performed by Sherrington and Sowton [2], who employed diluted blood as the perfusion fluid, and they found that an early constriction was followed by a dilatation, but that these results only occur with such strengths of choloroform solution as would actually abolish the heart-beat,

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* See also Embley and Martin and Schäfer and Scharlieb.

† Hill [1] says that on rotating an animal into the "feet down" position when under chloroform the blood gravitates into the dilated abdominal vessels, thus producing an alarming fall of blood-pressure. It is, however, difficult to assess the value of these experiments in the absence of any control of the strength of vapour employed. Embley has confirmed that a fall of pressure occurs in such circumstances, but gives no figures. Hill's own experimental data are scanty, and the pressure curve reproduced in Hewitt's "Anæsthetics" is open to question in respect of the methods adopted.

and that with ordinary clinical concentration these vessels are not affected one way or the other.

The Blood-pressure.—The measurement of the blood-pressure under chloroform anæsthesia gives us the information whether or no the circulation is being properly maintained, but affords no further information regarding the various factors, central and peripheral, of which it is the resultant. It is, however, important to know what is the normal course of the blood-pressure under chloroform, so that abnormal conditions may be recognized when they occur.

It is commonly said that chloroform reduces the blood-pressure, but this statement requires amplification.

The course of the blood-pressure is best studied in animals prepared as described in the footnote on p. 39, so that a record can be taken both before, at the commencement of, and during the administration.* It is then noted the first effect of the exhibition of the vapour, if this be moderately strong, is a rise of blood-pressure, as has already been described. One or more minutes may elapse before the pressure falls to about the pre-anæsthetic level, and thenceforth the animal may frequently be fully anæsthetized without the pressure falling any further or at any rate to any considerable degree; if, however, the full anæsthetizing strength of vapour is continued, undoubtedly the tendency is towards a gradual fall to a lower point. If strong concentrations of chloroform are required to anæsthetize the animal, then the blood-pressure may fall considerably, and the persistent administration of strong chloroform eventually reduces the pressure to a very low point.

The average of the normal blood-pressures of eighteen

* One notable effect of the administration of an anæsthetic to these animals is that the blood-pressure curve becomes comparatively smooth and free from violent fluctuations; previously to the administration the curve is frequently strikingly irregular, for every movement and probably every emotion has a disturbing effect.

cats registered before the administration of the anæsthetic, was found to be 133 mm., whilst the average of the blood-pressures in twenty-two cats under chloroform ranging from 0·5 to 2·0 per cent. at the moment of observation, and which had undergone slight operative procedures only, was 110·5 mm., a difference of 21·5 mm.

Clinical observations made during operations on man have shown considerable fluctuations in the blood-pressure, so that it becomes difficult to say what the normal pressure really is under such conditions. C. D. Edwards has tabulated the lowest blood-pressures recorded in a series of operations (some of them severe) performed under chloroform, and compared them with the normal in the same patients previous to operation; the average results are 92 mm. and 125 mm. respectively, showing an average drop of 33 mm. under operation, whilst in a corresponding series under ether the average maximum drop from normal was only 5 mm.* In five chloroform cases only out of seventeen the mean blood-pressure, calculated from the whole curve during the administration, was not below the pre-anæsthetic normal, and in each of these cases the anæsthesia was extremely light. These figures are instructive and definitely demonstrate a lowered pressure in operations under chloroform in man.

The operation cases which provided Edwards' material were probably not under a dead level of anæsthesia, for the chloroform vapour was not controlled mechanically, so it may be presumed some of the low pressures were unnecessarily low. The blood-pressure is undoubtedly better sustained when the vapour tension is maintained continuously at such a value as produces the required anæsthetic effect and no more, that is, of course, in the absence of severe operation shock.

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* The actual degree of fluctuation under ether averaged 35 mm., for the blood-pressure under ether was invariably *raised* at some time above the normal.

The blood-pressure, when lowered purely from excess of chloroform, recovers with fair readiness on reducing the vapour, but the recovery is not always as rapid as the fall. A lowered blood-pressure from shock requires separate consideration;* it is a more serious condition, for the pressure may be only restored with great difficulty and after a lengthy interval, or not at all.

* This subject hardly comes within the scope of this book.

CHAPTER V.

Pharmacology and Toxicology. (*Continued.*)

(*viii*) *The Kidneys.*

The Volume of Urine.—Renal activity under chloroform is largely determined by the flow of blood through the kidneys as under normal conditions, but, according to W. H. Thompson, not wholly so. The dilatation of the arterioles of the kidneys by chloroform, demonstrated by Embly, is at first neutralized by vaso-constrictor action of central nervous origin, and later more than neutralized by the fall of systemic pressure due to weakening of the heart, so that the final result is a diminution of the volume of the kidney, as was first observed by Kemp and Thomson, and confirmed by Buxton and Levy. All observers are agreed that under such circumstances the excretion of urine is diminished. Subsequently, on reversion to a lighter stage of anæsthesia, when the heart beats more strongly and distends the kidney with blood, then the existing vaso-dilatation is made evident by a distension of the kidney to above normal size.

The most complete experimental investigations into urinary flow have been made by W. H. Thompson. His conclusions are (1) "The volume of urine secreted by the kidneys is as a rule affected during chloroform narcosis in two ways. In the early stages, when anæsthesia is light, the quantity is frequently increased. During full anæsthesia, the secretion is always diminished, and may be suppressed. (2) The after-effect is invariably a great increase, which in certain periods may reach four times the normal volume for the

same period of time. The maximum output occurs about three hours after removal of the anæsthetic."

Levy* measured the quantity of urine drawn off by catheter within thirty minutes of the conclusion of forty operations under chloroform; nearly all the operations were abdominal, in female patients. The amount was found to be very variable, ranging from a minimum of 3 c.c. per hour of operation up to 63 c.c. per hour (which is about the normal for a healthy person), the average being 33 c.c. per hour. These results agree in the main with experimental observations, except that there was no discoverable relation between the degree of anæsthesia and the amount of urine excreted; nor did the conditions of the operation appear to have any controlling effect.

Thompson's observation of greatly increased flow of urine following the cessation of the administration is not confirmed by the clinical observations of Buxton and Levy; in fact the latter found on an average one-third less urine passed in the twenty-four hours after, than in the twenty-fours before, operation. Buxton and Levy point out that the counditions of an operation, purgation, vomiting, &c., may have an effect in lowering the excretion, but it is difficult to reconcile the contradiction between clinical and experimental observations.

The Solid Contents of Urine.—Thompson found that the nitrogen of the urine, which represents almost entirely the urea excreted, was usually diminished during the actual administration of chloroform, more so than the fall in the volume of urine; when the urine flow is increased in the post-chloroform periods the nitrogen may be likewise increased, but not in the same proportion. Thompson argues from this that the diminished renal activity cannot be wholly conditioned by the effect of the anæsthetic upon the blood flow through the organ. Buxton and Levy found the urine more

* Unpublished notes.

concentrated in the twenty-four hours after anæsthesia than before, the specific gravity being raised about one quarter, and inferred that the diminution of urine in this period is largely in respect of water.

The chlorides of the urine are largely and steadily increased during and after chloroform narcosis, reaching, during the fifth and sixth hours following the administration on an average, to ten times the normal amount. Control experiments under ether show an average increase of about three times the normal chlorine at a similar period, so that it cannot be said that the whole of the increase under chloroform is derived from that body.* The excretion of chlorides by the kidneys is a notoriously uncertain function, and conclusions from observations upon them must be accepted with caution, but the increase found by Thompson is large, and suggestive of the destruction of a portion of the chloroform within the body.

Abnormal Substances in Urine.—Albumen has been found in urine following operations by many observers, but opinions differ as to its frequency of incidence. Levy examined the forty catheter specimens referred to above for albumen, and its appearance was found to be a common event. Eight of the cases showed a trace of albumen before operation, but this is of frequent occurrence in females, especially those subject to pelvic disorders, and is not necessarily of renal origin. Excluding these he found albumen in twenty-one of the thirty-two remaining catheter specimens, that is in 65 per cent. of cases. The amount of albumen was not measured but fell under the following headings :—

Faint trace...	9
Marked trace	9
In considerable quantity	3
Total	21

When the albumen is abundant it may persist for a day or two, but eventually clears up entirely; the occa-

* W. H. Thompson.

sional persistence of albuminuria after the administration suggests that its presence is not due to a temporary vascular disturbance alone, but to some more permanent effect of the chloroform upon the kidneys.

When albumen is previously present then it may be increased in quantity, but not necessarily so, and as there is no record of harm resulting from chloroform in chronic kidney disease, the presence of albumen in the urine does not contra-indicate its administration.

Fatty infiltration and cloudy swelling has been observed in the cells of the tubules of the kidney, almost constantly according to Apperley, but only in patches, and largely restricted to the loops of Henlé. It would appear that such pathological change might well be associated with the escape of a varying proportion of albumen into the urine.

Urine passed after chloroform anæsthesia may have a weak reducing action upon Fehling's solution; this is not due to the presence of glucose, but the exact nature of the reducing agent has not been established.*

The occasional presence of small quantities of unaltered chloroform in urine has been referred to by Pohl and others, but the amount excreted in this way is negligible in quantity.

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* W. H. Thompson.

CHAPTER VI.

Some Physiological Considerations of Respiration.

The Respiratory Centre.—The respiratory nerve centre, which is responsible for the regulation of pulmonary ventilation, is itself affected mainly in two ways, which may be considered separately.

(1) Afferent nervous impulses.

These originate in great part as afferent impulses arising from the state of the lung itself, according as it is in partial collapse or distension, and conducted to the respiratory centre through the vagi, and it appears that nervous influences of this kind prevent over-action of the inspiratory movements, and further largely control the rate of the rhythm.

Nervous impulses reach the respiratory centre, however, otherwise than through the vagal route. Firstly, the centre is, within limits, under voluntary control in the conscious or sub-conscious subject. Secondly, strong sensory impulses produce powerful and rapid respiratory movements, simulating in volume the respirations of dyspnœa, and this effect may be observed in the course of a painful operative procedure when the anæsthesia is not very profound; it is not uncommon to observe a respiration rate of 40 or more per minute under such conditions. Thirdly, reflexes such as coughing and sneezing pass through the respiratory centre; they depend upon the excitability of the centre for their exhibition, and are entirely abolished when it is profoundly affected by an anæsthetic. Fourthly, respiration may be stimulated by sensory reflexes which are not painful, as, for instance, by rubbing the lips, or by dashing cold water on the face, or

even by blowing a stream of air over the face, and the centre responds to these stimuli even under moderately deep anæsthesia.

(2) The carbon dioxide tension in the blood.

The regulation of that function of the lungs which is expressed in the term "ventilation," is mainly effected by the carbon dioxide in the blood acting directly upon the respiratry centre : an excess of carbon dioxide stimulates the centre, leading to an increased amplitude of respiration, and also, but to a less degree, to an increased frequency ; a diminution of the carbon dioxide content of the blood acts in a reverse manner.

The excretion of CO_2 is a remarkably fine adjustment to the body needs, whereas the absorption of oxygen may be described as being only coarsely adjusted, the oxygen tension in the alveoli being normally in considerable excess of requirements ; as the utilization of oxygen and the production of CO_2 go hand in hand, it follows that the adjustment for the excretion of CO_2 not only provides at the same time for an increased oxygen supply, but actually anticipates the immediate necessity for it.

Acapnia.—If the breathing be restrained or held for a brief period, carbon dioxide will accumulate in the blood, and a sequence of deep respirations will be the result. On the other hand, a continued increase of ventilation leads to an increased elimination of carbon dioxide from the blood, which results in a diminution or, in extreme cases, an entire suppression of the respiration. Such a condition is termed "acapnia" ; when it occurs a further accumulation of carbon dioxide in the blood results, and a return to normal respiration is the consequence.

No doubt respiratory effects of this nature are occasionally observed under chloroform anæsthesia, following an increase of ventilation caused by excitement or painful operative procedures under light anæsthesia, but it is exceedingly doubtful if they ever need cause anxiety, normal respiration being necessarily resumed.

Yandell Henderson has, however, advanced a theory of a connection between acapnia and fatal syncope, not only in chloroform narcosis, but likewise during ether inhalation. Henderson's theory is based on the assumption that the respiratory centre becomes less sensitive to carbon dioxide in the blood during anæsthesia, and so the subject is more readily rendered acapnic, and less readily recovers from acapnia. There can be no question that the respiratory centre is depressed to *all* stimuli when deeply affected by chloroform, and its functions are entirely suppressed by an overdose, but even in such an extreme case its activities are not permanently abolished and are readily restored; but Henderson holds that syncope occurs essentially under light anæsthesia, following a period of hyperpnœa from excitement, and at this stage the respiratory centre is evidently little if at all affected.*

Henderson appears to consider that an acapnic pause in respiration under chloroform, if sufficiently prolonged, may lead to cardiac failure from asphyxia before the breathing is restored, even if the heart be not directly affected† by the deficiency of CO_2; and if such an extreme acapnic condition were conceivable the heart would continue to beat if artificial respiration were performed, and there would be no reason for its cessation.

Buckmaster and Gardner [1] claim to have demonstrated acapnic pauses following a period of hyperpnœa in animals, but it is probable that the pauses are in

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* Henderson's analyses of the CO_2 blood content under chloroform do not bear out his views, especially if we except those cases in which morphia has been administered also. Collinwood and Buswell find the alveolar CO_2 in cats to be about normal (average 5·7 per cent.) after 25 minutes moderate chloroform anæsthesia, but raised to an average of 7·1 per cent. after 45 minutes of very deep anæsthesia.

† It does not appear necessary to consider at length Henderson's contention that the heart is affected by acapnia. His results were probably an artefact derived from the extremely vigorous mechanical experimental method he employed, and in E. H. Starling's opinion there seems no reason to believe that the condition of acapnia had anything to do with the cardiac results observed.

reality due to an inspiratory spasm, or the "holding of the breath" so commonly observed in the early stages of the induction of anæsthesia (see p. 14). The statement that these pauses may have a fatal termination is apparently based on Henderson's views, for they do not adduce any evidence to this effect.*

Neither Henderson nor Buckmaster and Gardner appear to appreciate what a pure total respiratory failure implies from a clinical standpoint; a report of such a case is quoted below in order to illustrate the sequence of events:—

Male patient, readmitted to hospital in a semi-conscious condition. History of gunshot wound of head and fractured base of skull; he had been out of hospital only fourteen days.

Was suffering from intense headache, vomiting of cerebral type, and was found to have optic neuritis; temperature subnormal, pulse slow (45 to 50), heart and lungs apparently sound.

Patient had required several hypodermic injections of morphia on account of headache.

Immediate operation decided upon, viz., trephining. Was taken to theatre and anæsthetic commenced. Chloroform by open method (ʒss). At end of quarter of an hour patient was in theatre and was turned on his side in order that the operation (to back of occiput) might be begun. He promptly stopped breathing, and despite artificial respiration, *which was persevered in for two and a half hours before the heart's action ceased,* there was never any return of rhythmic or voluntary respiration.

Post mortem showed there was a septic hole in the bone beneath the healed wound—the cerebellar fossa was full of fluid —and the cerebellum contained an abscess holding about 4 to 5 oz. of thick pus. The respiratory failure was probably due to pressure of the pus upon the respiratory centre in the medulla, when the patient was turned over for the necessary operation to be done; as a matter of fact no operation at all was performed.

The heart was slightly hypertrophied but otherwise sound.

(*Private communication.*)

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* Buckmaster and Gardner [1] reproduce two tracings which show a definite temporary suppression of the respiration. In one the respiration comes to rest in the *inspiratory* phase, and so cannot be due to respiratory failure. The failure is in the expiratory phase in the second case, but it is quite sudden and is immediately consecutive to a marked exaggeration of tbe breathing; it is highly suggestive of a respiratory failure following cardiac syncope (q.v. p. 97).

Hewitt reports a similar case of operation for cerebral tumour, in which it was necessary to maintain artificial respiration for four hours, after which automatic breathing returned. Hewitt attributed the respiratory failure to the morphia which had been administered.

The conditions found in the foregoing cases are of extreme rarity, and are totally unlike those found in the ordinary forms of chloroform syncope. It is evident, therefore, that we must rule out of account any theory of primary respiratory failure (apart from that caused by overdosage) in considering the causes of syncope under chloroform.

Rebreathing.—Arising out of his theory of respiratory failure, Henderson has advocated rebreathing the expired air with its 4 per cent. of carbon dioxide, in order to raise the carbon dioxide tension in the alveolar atmosphere, and so provide additional stimulation to the respiratory centre, which he presumes to be weakened in its reaction to the normal carbon dioxide tension.

The average effect of raising the carbon dioxide tension in inspired air is shown in the subjoined table, taken from Haldane and Priestley's paper.

Percentage CO_2 in inspired air		Average depth of respirations in c.c		Average frequency of respirations per minute
0·04	...	673	...	14
0·79	...	739	...	14
2·02	...	863	...	15
3·07	...	1,216	...	15
5·14	...	1,771	...	19
6·02	...	2,104	...	27

Pembrey and Shipway have estimated the percentage of carbon dioxide re-inhaled in various methods of administering ether. The highest percentage resulted from breathing to and fro into a bag, a method not employed in connection with chloroform. In the case of a closely applied fabric mask of the Schimmelbusch pattern, with an internal capacity of about 250 c.c., the air contained from 2·5 per cent. to 3·1 per cent. under ether anæsthesia. Considerable respiratory distress was

caused to a conscious man from inhaling 6 per cent. carbon dioxide, but 3 per cent. produced no distress.

The capacity of a closely applied chloroform fabric mask would be less than that of an "open ether" mask, so that the CO_2 content would be lower, but evidently appreciable; this would also apply with any closely applied inhaler mask, and in such cases we may expect to find the ventilation increased somewhat above the normal. In the cases of a purely "open" chloroform mask which does not touch the face, there would be practically no re-breathing at all.

In view of the fact that Henderson's contentions regarding respiratory failure do not appear tenable, re-breathing of expired carbon dioxide would not seem to have much scope for application in chloroform anæsthesia; when respiration weakens from an excess of chloroform the indication is to reduce the chloroform. If breathing becomes weak apart from any recognizable cause, and fails to revive by such a common expedient as rubbing the lips, rebreathing may probably have an effect; in such a case a confined atmosphere might be induced by wrapping a towel round, but not touching the mask, or placing a hollow cylinder of paper over the mask. Possibly again rebreathing may assist free respiration in the early stages of the induction of anæsthesia and help to avoid the restraint of breathing which is frequently a feature at that period, but whether the complication thus introduced is warranted is a matter for personal predilection.

I have seen a practice made of drawing a blanket round the face of a person recovering from an anæsthetic, with the object of partially retaining the expired air about the face for the purpose of keeping the face warm. In reality I think the benefit is derived from rebreathing the expired carbon dioxide, whereby the more rapid exhalation of the anæsthetic is promoted owing to increased pulmonary ventilation; this procedure would thus appear to be desirable.

Rebreathing of course involves some deprivation of

oxygen, but probably this is not serious in an only partly confined space, but the deprivation may readily become serious if expired air be continually re-inhaled. The observation made by Brodie and Dixon must likewise be borne in mind that the inhalation of even as little as 3 per cent. of carbon dioxide tends to contract the bronchioles, so that it is possible that the inhalation of this quantity may lead to a noisy and laboured type of breathing even if the supply of oxygen be not deficient.

Rate of Pulmonary Ventilation.—The rate of intake of air has to be considered in connection with the various methods of administration of chloroform. About 500 c.c. of air are inhaled some sixteen times per minute during quiet breathing in an adult, that is, about 8 litres per minute. The rate of ventilation in anæsthesia will vary according to changes in the depth and rate of respiration; it may be diminished to any extent down to actual suppression by the anæsthetic, but the extent of its increase is of course limited. Extreme stimulation of the respiratory centre will raise the intake to 50 litres per minute or more (see Haldane and Priestley's table, p. 52), but this rate is rarely approached under conditions of chloroform anæsthesia; from personal observation I should judge that the maximum intake likely to be met with would be about 24 litres per minute with a volume of 800 c.c. per inspiration, and a respiration rate of 30 per minute.

Rate of Flow during Inspiration.—A knowledge of the rate of intake during inspiration is important from a physical standpoint; this is necessarily higher than the rate of ventilation, of which the unit of time includes both the inspiratory and expiratory phases.* I have made estimations of this rate of inflow or "force of inspiration," in persons under chloroform by means of

* It is evident that these two rates have been frequently confused in calculations of rates of evaporation, and in calibrating the atmospheric flow of inhalers.

a special kind of apparatus, originally designed as part of an inhaler;* these estimations are tabulated below.

	c.c. per second	Equivalent rate in litres per minute
Forcible breathing ...	700 to 900 ...	42 to 54
Strong „ ...	500 „ 700 ...	30 „ 42
Moderate „ ...	350 „ 500 ...	21 „ 30
Weak „ ...	250 „ 350 ...	15 „ 21
Very weak „ ...	Under 250 ...	Under 15

The application of these figures will become apparent in the chapter relating to methods of administration.

* Levy [7].

CHAPTER VII.

Deprivation of Oxygen and Asphyxia.

The absorption of oxygen by the blood is not governed by the laws of simple solution, for it enters into a loose combination with hæmoglobin. The blood is practically saturated with oxygen at the low partial oxygen pressure of 100 mm. (equivalent to the average normal oxygen content of alveolar air, viz., 13·2 per cent.); at 80 mm. partial pressure the blood is still 95 per cent. saturated, and the alveolar oxygen may be reduced to 50 mm. pressure (6·5 per cent.) and yet the blood will still be 80 per cent. saturated, and under ordinary circumstances there may be no evidence of cyanosis at this pressure.* It follows that a considerable deprivation of air may occur without reducing the oxygen in the blood to any serious extent, and a further deprivation of oxygen may fail to produce cyanosis.

The deprivation of oxygen which is consequent upon the inhalation of chloroform vapour may be considered here, for the space occupied by the vapour displaces an equivalent amount of air, and consequently a proportion of oxygen. A vapour of 2 per cent. concentration present in the alveoli (which would be conditioned by the actual inhalation of a higher percentage) would displace only a very small proportion of the normal alveolar oxygen; it would reduce it in fact from 13·2 per cent. to 12·9 per cent. Even a 6 per cent. vapour would only reduce the oxygen to 12·4 per cent., or 94 mm.

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* These figures take into account the 40 mm. tension of CO_2 which is normally existent in arterial blood, and which exerts a restraining influence upon the combining powers of oxygen and hæmoglobin.

pressure. We may therefore be assured that the presence of an anæsthetic proportion of chloroform vapour in the lungs is negligible as regards its displacement of oxygen.

An *extreme* deprivation of oxygen powerfully stimulates the respiratory centre, together with a great part of the central nervous system.* This is well exemplified in cases of sudden circulatory failure, such as may occur from the bursting of an aneurysm (A. Wilson), or from an extensive incised wound of the heart, or from sudden cardiac failure in any form; the respiration in such cases becomes increased in amplitude but not in frequency, and after a brief period ceases entirely from failure of the centre (fig. 3). The stimulation extends to all motor centres, causing general muscular convulsions, which are of a powerful nature in the unanæsthetized subject and which are frequently evident, though modified in a lightly anæsthetized one.

The sequence of events in a complete, or nearly complete deprivation of air, or "asphyxial" condition, is as follows: The respiratory movements are exaggerated in the first instance by an accumulation of CO_2 in the blood, and later more intensely by want of oxygen. These later respiratory efforts have a strong expiratory tendency and are accompanied or frequently followed by a general muscular spasm. Following this spasm, or at about the same time, the heart fails from want of oxygen, and the respirations cease from exhaustion of the respiratory centre; a long pause then ensues terminating in a series of isolated gasps at long intervals. Under anæsthetics the process is modified†—in an animal which is fully under an anæsthetic the respirations are in the final stage only slightly increased in volume, and, especially under chloroform, the stage of asphyxial spasm may be entirely suppressed. The spasm is almost or entirely absent when the animal has

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* See note on p. 98.

† Levy [6].

been inhaling any concentration of vapour over 1 per cent. of chloroform, but it is never entirely suppressed under ether.

By causing an animal to rebreathe the contents of a small bag through a tube inserted into its trachea until asphyxiation takes place, and estimating the amount of oxygen left in the bag on cessation of respiration, a measure of the animal's resistance to asphyxia is obtained.

In four cats under chloroform the residual oxygen in the bag was as follows:—

	Percentage of chloroform	Residue of oxygen in bag Per cent.
(1)	1·8	4·5 O_2
(2)	1·8	4·2 „
(3)	2·0	4·5 „
(4)	0·8	4·0 „
		4·3 average

This average figure of 4·3 per cent. corresponds closely with the figure given by Paul Bert [4] for the lowest respirable percentage of oxygen for the cat, viz., 4·4 per cent., so we may take it that the anæsthetized cat is not more susceptible to oxygen want than the cat not under an anæsthetic.*

Richet [1] has stated that animals which have been asphyxiated under chloroform can always be restored by artificial respiration for some minutes after cessation of respiration. I have, however, observed instances both under chloroform (and more frequently under ether), in which the heart-beat could not be restored in

* Under ether the oxygen left in the bag was greater in amount than under chloroform—the average of seven experiments was 6 per cent. oxygen, which is considerably higher than Bert's lowest respirable percentage. These figures are in agreement with and are confirmed by the final CO_2 content of the bag, viz., an average of 10·2 per cent. in the case of chloroform and an average of 8·0 per cent. in the case of ether. It is thus evident that an animal under ether is more susceptible to want of oxygen than one under chloroform. This was confirmed by observations upon the time taken before the breathing stopped in the same animal asphyxiated alternately under ether and chloroform.

this way after its failure from asphyxia, and needless to add the respiration likewise.

It would appear from these observations that the heart-beat and respirations may be suppressed to extinction by asphyxia under chloroform with little or no objective symptoms beyond cyanosis; that is to say, the subject may quietly and rapidly undergo suffocation to the point of death unless the obstruction to respiration is recognized by the cyanosis and its cause expeditiously removed. Asphyxia is thus an insidious condition under chloroform and requires careful watching for; no doubt it is seldom allowed to proceed to an extreme condition, and even then is amenable to restorative measures, but an occasion may arise in which no procedure short of cardiac massage is capable of restoring the heart's function.

Much stress has been laid upon the danger of a partial "intercurrent" asphyxia, more especially by the Hyderabad Commission and the late Sir Frederick Hewitt, but it is difficult to discover upon what actual facts, either experimental or clinical, they base their conclusions. So far as a single experimental result warrants a conclusion, I must admit a limited danger from an incomplete asphyxial condition, possibly accentuated during recovery from asphyxia; this matter is dealt with in considering the causes of fibrillation of the ventricles (p. 31). In any case a condition of partial asphyxia cannot be a desirable one; further, it must be associated with imperfect absorption of the anæsthetic, and it is therefore wise to adopt every precaution to avoid any impediment to free respiration.

The Administration of Oxygen.—In the course of normal pulmonary ventilation with an effective circulation, the oxygen in the inhaled air is more than sufficient to provide oxygen to the tissues, as has already been explained, and it is therefore evident that the administration of an excess of oxygen can serve no useful purpose under normal conditions; it can at most add two volumes per cent. to the oxygen in the blood.

Buckmaster and Gardner [2] have shown in their experiments upon animals that a considerable deficit of oxygen may exist in the blood in chloroform anæsthesia, but their contention that this is due to chloroform exercising a restraint upon the combining power of oxygen and hæmoglobin cannot be regarded as proved (p. 19). There can be no question, however, that in chloroform anæsthesia the blood may become darker in colour than normal, and this fact appears to be accounted for by a depression of the respiration (although Buckmaster and Gardner deny this), and further and perhaps more especially by a lowered blood-pressure. It is a common experience that in the case of a carefully regulated administration of chloroform the blood-pressure is well sustained and the blood remains of a good colour; it is only when an unnecessary amount of chloroform is introduced into the blood by irregular administration that the blood becomes dark, and it is only in extreme instances of this occurrence that actual cyanosis appears. The attention of the anæsthetist should therefore be directed towards maintaining a continuous supply of vapour of the correct concentration rather than to the administration of pure oxygen for the purpose of keeping the blood efficiently oxygenated.

Oxygen gas may sometimes be administered with advantage for the relief of an unavoidable asphyxial condition. It is a valuable agent to employ in cases of emergency, and should be so regarded; the tendency which has developed in recent years to employ it almost as a routine adjunct is, I think, to be deprecated, for it then becomes a mere complication which tends to disguise a faulty method. Special conditions are, however, liable to arise, in which the process of oxygenation may meet with interference; in such cases the first indication is naturally to remove the cause of the condition if this be possible, but if not possible, then the administration of oxygen comes under consideration.

The use of oxygen is indicated essentially when the pulmonary ventilation is seriously and unavoidably reduced, either by deficient respiratory movements, or by an obstruction to the respiration; in such cases the administration of an excess of oxygen in the atmospheric air naturally tends to raise the oxygen tension in the pulmonary alveoli, and relieves the condition of asphyxia.

The ventilation of the lungs may be seriously reduced in various ways; an excessive dose of anæsthetic may be the cause, and the induction of deep anæsthesia may be intentional by reason of the exigencies of an operation; or the respiration may be adversely affected through operative procedures, as it frequently is in brain operations. Under such conditions oxygen may be administered with benefit.

Respiration may be obstructed mechanically in many ways (see p. 143); the use of oxygen in this connection is obviously a last resort, but when all other means fail it should be employed without hesitation.

When cyanosis has been pre-existent, apart from the administration of an anæsthetic, whether arising from respiratory obstruction or an affection of the lungs, then obviously inhalation anæsthesia would not be a method of choice, but if no other be available, then oxygen should by all means be given as an adjunct to maintain the patient in good condition.

The plasma is practically negligible as an oxygen carrier at normal alveolar oxygen tensions. At an oxygen pressure of 760 mm. (pure oxygen), however, it takes up an appreciable quantity of the gas into solution (2·2 c.c. of oxygen per 100 c.c. plasma); therefore after severe hæmorrhage, when the quantity of hæmoglobin in the residue of blood may be insufficient to supply the body want, saturation of the plasma by the inhalation of pure oxygen may no doubt be a means of bringing a small additional supply to the tissues and should prove of value as a temporary measure until transfusion of blood can be performed.

In opposition to the conclusions of Brüning, Gwathmey maintains that the inhalation of an anæsthetic vapour with pure oxygen as a carrier instead of atmospheric air is a safeguard against death by overdosage; apparently he claims that it is less toxic to the heart and respiratory centre. Gwathmey's statement of his results is really valueless from a scientific standpoint, for the strength of the vapour administered in his parellel series of experiments was not controlled by measurement, and there is abundant evidence that it did in fact vary enormously; indeed his claim as to the relative "safety" of oxygen with anæsthetics rests on such an insecure basis that it cannot be seriously considered.*

* It is probable that in overdosage with a chloroform-oxygen atmosphere the heart will beat longer after respiratory failure than when a chloroform-air atmosphere is employed; restoration by artificial respiration might therefore be longer delayed, but this does not appear to be the point to which Gwathmey refers.

CHAPTER VIII.

Consideration of the Mechanism of the Absorption and Elimination of Chloroform.

The method of introducing an anæsthetic vapour into the blood by inhalation possesses at least two salient advantages which account for the dominant position that it occupies at present. The first is its performance without the aid of surgical procedure, the second its capacity for rapid adjustment. The pulmonary route is a physiological device for the easy passage of gases to and fro between the alveoli of the lungs and the blood, so that absorption is rapid, and excretion hardly less so. There is a delicate response to a little increase or a little decrease in the concentration of the vapour inhaled, and this concentration may be so readily adjusted, that it is difficult to conceive of any method which is likely to rival it in these relations.

The successful application of the inhalation method is essentially dependent upon the free performance of the respiratory functions. An obstruction of the air-way must, more or less according to its degree, impair the perfection of the result, and the administration under such circumstances will at least be attended with difficulty. So also a circulation which is defective to the degree of diminishing the vascular irrigation of the lungs will certainly discount its successful employment; it is evident that in those extreme cases in which the blood is unable to become efficiently oxygenated, the absorption and excretion of anæsthetic vapour is likewise impeded and cannot proceed so smoothly and rapidly as in normal conditions. Whenever, therefore,

dyspnœa or cyanosis is present, whether from central circulatory disturbance, or from an affection of the lung, it should certainly be considered whether some other method than inhalation anæsthesia would not be preferable;* otherwise in the great majority of cases it is at least possible and effective.

An anæsthetic vapour has to obtain access to the central nervous system in order to exert its anæsthetic effect, and the sequence of the stages of the transfer is as follows:—

(1) *From the Atmosphere to the Pulmonary Alveoli.*

The Effect of a Change in Ventilation.—The pulmonary alveoli are kept charged with vapour by the respiratory movements, but the proportion of vapour in the alveoli will be less than that in the inspired air so long as chloroform is being absorbed by the blood. The tidal air, it must be remembered does not sweep out the alveoli—it merely diffuses into the complemental and residual pulmonary contents, which combined measure about five times the average volume of tidal air. The actual proportion of alveolar vapour, therefore, is influenced to a considerable extent by the rate of pulmonary "ventilation,"† for an increase of ventilation effects a more rapid replacement of a depleted alveolar atmosphere by a fresh one; so, on the other hand, a diminished ventilation results in an undercharge of alveolar vapour. It thus happens that during the stages of absorption of chloroform vapour, a change of ventilation has a notable effect upon the progress of anæsthesia, so that the effect of a given vapour strength in the inhaled atmosphere can only be judged on the basis of an average rate of ventilation; the effect is accelerated with a *plus* rate of ventilation, and retarded with a *minus* rate of ventilation.

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* An estimation of the alveolar CO_2 might be of some assistance; a lowered CO_2 content generally indicates an impaired gaseous exchange.

† "Ventilation" is generally expressed in c.c. per minute, being the product of the rate of respiration per minute and the volume of the tidal air.

When absorption by the blood becomes less active, as it does in the later stages of an administration, then the alveolar vapour is less depleted, and the effect of a change of ventilation becomes less notable.

The Dead Space.—The alveolar vapour is likewise kept consistently somewhat lower than that of the inspired atmosphere, by reason of the intervention of the anatomical "dead space."

The whole of the inspired air does not actually enter the lungs, or the whole of the expired air reach the exterior with each respiratory movement. A portion is held up in the avenues of approach, that is, the tracheal and bronchial passages, which are estimated to measure in an average adult about 140 c.c. These passages constitute a "dead space" from which no absorption takes place; it is considerably augmented by the cubic capacity of the nasal and pharyngeal cavities.

Let us presume that at the very commencement of the induction of anæsthesia there are 2 vols. of chloroform vapour to every 98 vols. of air, that the dead space measures 150 c.c., that the complemental and residual air together measure 2,500 c.c., and that the tidal air is 500 c.c. The first inspiration brings 350 c.c. (500 c.c. less 150 c.c. dead space) of mixture containing 7 c.c. of vapour, into the lungs; this mixes with 2,500 c.c. of lung air, forming a mixture of 0·23 per cent. vapour. Without the dead space the mixture would be 0·333 per cent. (i.e., 10 c.c. of vapour in 3,000 c.c. mixture), so that it is seen that a dead space materially retards the rise of vapour tension in the lungs; and for an inverse reason excretion of vapour from the blood is retarded on account of the dead space hindering the access of pure air to the lungs.

The influence of the dead space is obviously only of real importance during changes of anæsthetic state, that is during active absorption or excretion.

The dead space becomes artificially increased when breathing takes place through parts of apparatus in direct continuity with the respiratory passages, and an

effect is thus exerted which is additional to that exerted by the anatomical dead space alone.

(2) *The Transfer of Vapour from the Pulmonary Alveoli to the Blood.*

Absorption by the Blood.—The physiological mechanism of the lungs affords naturally extremely favourable conditions for rapid absorption of a respirable vapour. The alveolar walls on the one hand present a vast surface to the atmosphere, and on the other hand a vast vascular surface is presented by the innumerable tiny streaks of blood flowing through the capillaries. The extremely thin alveolar and capillary walls, so far as is known, are entirely passive, and neither obstruct nor expedite the free interchange of vapour (Cushny).

The laws governing the absorption of a gas or vapour by water or any liquid upon which it exerts no chemical action may be simply stated. The amount taken up is dependent on (1) the specific nature of the gas (i.e., its innate solubility, (2) the temperature of the liquid, and (3) the pressure under which the absorption is effected.

For the purpose of considering an anæsthetic problem the temperature of the fluid under consideration may be regarded as practically a constant, for the temperature of the blood is always at 98·4° F. or thereabouts, the variation being negligible. The pressure under which vapour absorption is effected is, however, variable, and, from the anæsthetic point of view, all-important. We have already seen that within the range of ordinary anæsthetizing vapour tensions, the absorption by blood is proportional to the pressure (p. 6), and another important physical law may now be stated—*the rate of absorption is proportional to the difference of pressure existing between the vapour in the alveoli and in the blood.*

The principles applying to absorption likewise apply to elimination; if the atmospheric partial pressure is reduced the vapour is evolved from solution until an

equality of tension between the vapour in the solvent and the vapour in the atmosphere is established. If the atmospheric partial pressure is reduced to nothing, then the gas is entirely eliminated from solution.

Deep breathting promotes absorption, firstly, by distending the alveoli and increasing the absorbent area; secondly, by increasing the negative pressure in the thorax and thus inducing a higher rate of flow of blood through the capillaries of the lungs.

(3) *The Transfer from the Blood to the Tissues.*

The nerve centres and other tissues of the body are affected according to the tension of the vapour dissolved in the fluid with which they are bathed. This is well exemplified in Sherrington and Sowton's experiment of perfusion of the mammalian heart with an oxygenated solution containing chloroform: in these circumstances the contraction of the ventricles is affected in the most delicate fashion by a slight variation of the concentration of the chloroform in the solution—the contractions become weakened with a slight increase of chloroform, strengthened with a slight decrease, and rapidly recover their full force of contraction on perfusion with saline free from chloroform. It may be inferred by analogy, and is indeed evident from clinical experience, that the nervous mechanism of the body is affected in the same way, that is, in proportion to the vapour tension of the anæsthetic in the blood.

The blood is the carrier which must be charged with chloroform at a tension sufficient to affect the centres of consciousness and sensation to the required degree; this is termed the "anæsthetizing tension," and it lies within certain limits which are evidently narrow but not yet exactly ascertained. Below the requisite tension the anæsthetic result is imperfect, and above it the depression extends to vital mechanisms. If the blood alone were to be charged up to an anæsthetizing tension this would not take very long, but the blood is only about one-twentieth of the body-weight, and in order that the

blood should be brought to a steady value of vapour tension and maintained at it, it is evidently necessary that pressure equilibrium must be established not only between the blood and the alveolar atmosphere on the one hand, but also between the blood and the body tissues on the other.

The conditions of absorption of vapour by the solid tissues do not lend themselves readily to investigation,* but such knowledge as we possess allows us to formulate certain broad assumptions. It may be assumed that the transfer of vapour from the blood to solid tissues is a slower process than the transfer from the alveolar atmosphere to blood, and that the relation between the reverse processes is the same. It would follow that during absorption the vapour tension in the blood is always higher, and often much higher in the blood than in the tissues, and that the tissues continually tend to deplete the blood until the theoretical condition of equilibrium is attained. It will be evident, having in view the large relative bulk of the tissues, that the establishment of a true equilibrium must be a lengthy process, and it may well be questioned whether it is attained within the average duration of an operation.

The introduction of the amount of vapour requisite to bring the blood to an anæsthetizing tension cannot in practice be attained by the administration of a vapour of a like atmospheric tension, for such a procedure would occupy far too much time; owing to the low concentration only very little chloroform would be absorbed by the blood at each passage through the pulmonary capillaries. This would not be the only cause of delay; so long as active absorption continues the alveolar vapour is being depleted, and it is kept at a tension which is constantly and materially lower than that in the atmosphere administered. It is evident, when the atmospheric tension is the minimum anæs-

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* The relative absorptive properties of some tissues is shown on p. 81.

thetizing tension, it can only be as the solid tissues become saturated, a very slow and gradual process, that an approach is made to pressure equilibrium throughout, and a satisfactory anæsthetic state established. In practice, therefore, the time taken for the induction of anæsthesia is shortened by the administration of chloroform at a higher tension than that aimed at in the blood, thereby not only effecting a more rapid absorption, according to the law just stated (p. 66), but likewise continuously compensating the blood for depletion by the tissues; in this way the blood is soon brought to an anæsthetizing tension and maintained at it, before the solid tissues have in fact become saturated.

As soon as the blood reaches a full anæsthetizing pressure, then the continued administration of a strong vapour is unnecessary and, in fact, detrimental, for it would raise the blood tension above what is required and an "over-dose" would be introduced. It is therefore necessary to reduce the vapour strength progressively but gradually until a condition approaching equilibrium is attained, when the vapour tension exceeds very little the blood tension, or perhaps eventually not at all.

From a theoretical standpoint it is important to realize that the employment of a weaker vapour, and that a continually decreasing one, for the maintenance of anæsthesia than for its induction, is fully explicable on physical grounds, and that there is no reason to presume a progressive susceptibility of the nerve centres to the influence of chloroform.

Recovery from the Effect of a Volatile Anæsthetic.—It will now be evident that if the anæsthetic is withdrawn very early in the administration, as during induction, the blood is depleted not only by exhalation from the lungs, but also, although to a less degree, by absorption *into* the unsaturated body tissues, and hence the patient rapidly recovers consciousness. When, however, a condition approaching equilibrium has been attained,

as towards the completion of an administration, the vapour is exhaled from the lungs similarly on withdrawing the anæsthetic, but there is then a large store of vapour in the tissues which will be transferred to the blood as this is depleted by exhalation and as its vapour tension falls, and so it results that anæsthesia under such circumstances lightens more slowly and a longer time is taken to regain the fully conscious state. The rapidity with which patients recover when just fully anæsthetized, and especially when only partially anæsthetized, may well be explained on these physical grounds, although our first inclination might tend to a physiological solution of the problem.

From the foregoing considerations it becomes apparent that the successful administration of a volatile anæsthetic to a patient with a free airway, and in other respects a suitable subject, must depend to a great extent upon the power of adjusting the strength of the vapour according to the requirements of the moment, and having adjusted it, the power of maintaining it at that strength so long as may be required. In other words, the administrator must acquire (1) control of the strength of the vapour, (2) control of continuity of administration.

The administration of an anæsthetic vapour is thus largely a physical process, far more so than is generally appreciated, and a grasp of the above-mentioned principles will carry the student a long way towards the successful attainment of his object.

Experimental Observations upon the Absorption and Elimination of Chloroform.—The experimental observations on the mechanism of the exchange of vapour between the air and the blood are limited in number, but are of considerable interest.

Brodie and Widdows administered a known percentage of chloroform to cats for a period of ten minutes, and estimated the chloroform in the expired air at regular intervals; measurement of the volume of expired

air provided data for calculating the chloroform absorbed. They found the greatest absorption took place in the first two minutes, in the second minute greater as a rule than in the first.* Thenceforth the absorption became progressively less, but at the end of ten minutes a considerable amount of chloroform was still being absorbed; that is to say, equilibrium was not established at the end of ten minutes, when the animals were generally well anæsthetized. Generally speaking the total amount absorbed in the ten minutes varied with the concentration of the vapour administered, but by no means in proportion to that concentration, the results being no doubt affected by the rate of ventilation.

The proportion of chloroform absorbed to that inhaled in five experiments may be tabulated thus:—

Percentage inhaled	Proportion of chloroform absorbed to total inhaled in ten minutes
1·64	0·42
1·8	0·32
2·0	0·47
2·3	0·63
2·78	0·54

Roughly stated we may say that with a vapour under 2 per cent. less than one-half, and with one over 2 per cent. more than one-half of the vapour is absorbed within the first ten minutes of the continuous administration of vapour of a constant percentage.

These results of Brodie and Widdows conform on the whole to the laws of absorption already stated (p. 66).

Vernon Harcourt [3] made some observations upon the chloroform expired by the human subject in the course of operations, and the following example of his results agrees with those of Brodie and Widdows in the progressive reduction of absorption, despite a progressive increase of the percentage of vapour administered.

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* The excess absorption in the second minute may well be attributed to the delay in getting the lungs filled with the full atmospheric percentage in the first minute.

Samples collected at intervals of about 6 minutes from beginning to end of the administration.

Percentage of chloroform in air		Percentage of chloroform administered which was	
Inhaled	Exhaled	Breathed out	Retained
1·03	0·41	40	60
1·4	0·69	49	51
1·93	1·29	67	33
1·66	1·22	73	27
2·14	1·63	76	24
2·06	1·61	78	22
1·15	0·90	78	22
2·23	1·40	63	37*
1·44	1·02	71	29
0·80	0·59	72	28

* *Note.*—At this time owing to the exigencies of the operation the mask was twice removed.

The whole time occupied was sixty-two minutes; the quantity of chloroform used was 25 c.cm. (6½ dr.); the average percentage administered over the whole time was 1·6 per cent. Of the chloroform administered one-third had been retained when administration ceased. Of three other experiments one confirms the foregoing results; in the remaining two the progressive reduction was not so marked.

It is notable that at the end of sixty-two minutes absorption was still taking place, although the intake was reduced to 0·8 per cent. vapour; the body would not therefore be charged up to this vapour tension,* but it is possible that this determination may be inexact.

B. J. Collingwood estimated the proportion of chloroform expired by cats after the elapse of a lengthy period of inhalation. He induced anæsthesia with 2 per cent. chloroform and then maintained it with 1·3 per cent. His results were as follows:—

	Inspired Per cent.	Expired Per cent.
Cat after 1 hour 20 minutes anæsthesia	1·3	1·2
„ 1 „ 50 „ „	1·3	1·4
„ 1 „ 23 „ „	1·3	1·3

* According to Moore and Roaf's tables a vapour tension of 0·8 per cent. would charge 100 grammes of serum with about 23 milligrammes of chloroform, and hæmoglobin solution to the extent of 25 milligrammes per 100 grammes at 40° C. (*cf.* p. 80).

These results imply that the body was saturated at the vapour tension of 1·3 per cent. of an atmosphere (= 9·9 mm.), and that no further absorption was taking place after the elapse of the time stated, the 1·3 per cent. tension in the air merely serving to "cork up" the body dose and prevent its exhalation.*

Elimination after Cessation of Administration.—On cessation of the administration the process of absorption is reversed—that is, elimination proceeds rapidly at first, followed by a gradual slowing off as the tension in the blood falls. The following estimations of the chloroform in the blood made during recovery from narcosis exemplify these facts (Nicloux [2]).

	Time after cessation of administration	Milligrammes per 100 cc. of blood
(1)	0 minutes	54
	1 „	35
	2 „	29
	5 „	25·5
	15 „	20·5
	30 „	18
	60 „	13·5
(2)	0 „	59·5
	30 „	23
	1 hour	16
	3 hours	7·5
	7 „	1·5

Generally speaking about half the quantity in the blood is exhaled in the first five minutes, but a trace of chloroform may remain unexhaled even several hours later. Nicloux gives no data as to the time which had been taken to introduce the chloroform into the body, but it may be presumed that the process of elimination will be longer after a long administration owing to the more effective charging up of the tissues with chloroform in the course of time, and shorter if the anæsthesia has been induced rapidly.

* According to Moore and Roaf a vapour tension of 9·9 m.m. causes 48 mgm. of chloroform to dissolve in 100 grammes of serum. Possibly, therefore, it is a fact that the body may be saturated with chloroform up to this tension without causing a cessation of respiration, but Collingwood's results require further confirmation (*cf.* p. 80).

CHAPTER IX.

The Dosage of Chloroform.

It will be recognized from what has already been written that the term "dose" of a volatile anæsthetic has a strictly limited application. In the case of a solid drug (e.g., morphia) which is introduced into the body by the mouth or under the skin, the amount administered is the same as the amount retained in the body, which remains potent until it is destroyed within the body or excreted. The "dose" of a volatile anæsthetic is properly speaking the amount which the body contains at a given moment, and the term should not be applied, as is commonly the case, to the amount which is used in the course of administration. The two amounts are entirely independent, and may be widely different, for, not only is some of the vapour continually exhaled from the lungs, even during the period of most active absorption, and in later stages much more largely, but likewise, as in the administration on ordinary fabric masks, the quantity of anæsthetic used is generally greatly in excess of the vapour which is inhaled, a proportion more or less large according to the method employed, being evaporated into the surrounding atmosphere. It is better therefore to avoid as far as possible the term "dose," in relation to the amount administered, and speak of vapours as being administered either "weak" or "strong" or else as measured in percentage terms. The terms "overdose" and "under-dose," however, refer to the amount of chloroform contained in the body and are expressions which may be conveniently retained.

It has been explained in the foregoing chapter how

the retention of the charge of chloroform is retained in the tissues of the body by the maintenance of a suitable vapour tension in the pulmonary alveoli, and how this charge is subject to reduction only by a decrease in this alveolar vapour tension. Possibly this is not exactly the case, for a proportion may be destroyed in the body, but the evidence in respect of this fact is contradictory and cannot be regarded as settled at the present moment. A little of the vapour is no doubt excreted by the kidneys, but so little as to be of no practical account.

The Percentage of Chloroform Vapour which is requisite to induce Anæsthesia.—Snow concluded that a maximum of 4 per cent. chloroform vapour was permissible and should be available for administration in order to induce anæsthesia.

Paul Bert [2] at first considered from clinical tests that a maximum of 1·5 per cent. was sufficient for this purpose, but Aubeau subsequently found that a maximum of 2 per cent. should be available. The Special Chloroform Committee of the British Medical Association arrived at a conclusion in agreement with Aubeau, viz., that a percentage of 2 per cent. eventually produces full surgical anæsthesia in all subjects, and that this percentage should be adopted as a maximum on the grounds of safety, that is in their view, the avoidance of a risk of overdosage. This conclusion was arrived at as a result of the extensive clinical use of an inhaler designed by Prof. A. G. Vernon Harcourt [4]. (See p. 121.) The readings of this instrument are not, however, sufficiently reliable to afford the precise data required for drawing scientific conclusions.

There is, it is true, little question but that 2 per cent. will induce surgical anæsthesia in most cases, *given sufficient time of action,* but the factor of convenience puts a limit to the time which can be allowed for induction. H. C. Crouch tested the Harcourt inhaler under physical conditions which precluded the evolution of an excess of vapour from fortuitous circumstances in nine surgical cases, and he found the results very un-

satisfactory with an indicated 2 per cent. limit. His results in brief were as follows :—

No.	Case Sex	Age	Duration of induction period with a 2 per cent. vapour limit	Result of induction
1	F.	22	10 minutes	Satisfactory
2	M.	25	29 „	Incomplete
3	M.	36	21 „	Incomplete
4	F.	40	20 „	Failure
5	M.	18	13 „	Satisfactory
6	M.	17	14 „	Incomplete
7	F.	12	10 „	Satisfactory
8	F.	23	15 „	Failure
9	M.	31	21 „	Incomplete

Thus only two cases were satisfactorily anæsthetized within a limit of ten minutes, when the conditions of inhalation were under proper physical control. The results obtained by the instrument employed as in ordinary clinical usage and upon which the Chloroform Committee based their report, cannot therefore be accepted as reliable.*

Levy [11] investigated the same subject, employing an inhaler which yielded percentages of vapour which were not liable to fluctuation (see p. 123), and has reported the details of ten administrations which were conducted with every possible attention to detail in order to secure accuracy.

No.	Case Sex	Age	Duration of induction period with a 2 per cent. limit	Result of induction
1	F.	47	5 minutes	Satisfactory
2	F.	50	11½ „	Incomplete
3	F.	44	10½ „	Satisfactory
4	F-	29	13½ „	Incomplete
5	M.	29	14 „	Failure
6	F.	24	14¾ „	Satisfactory
7	F.	43	15½ „	Satisfactory
8	F.	26	16 „	Satisfactory
9	M.	36	22 „	Incomplete
10	F.	54	20½ „	Incomplete

Taking ten minutes as the limit of convenience for the induction of complete chloroform anæsthesia, none

* Modifications of this instrument were introduced at later date which possibly tend to accelerate the induction.

of the above cases with the exception of No. 1 can be regarded as entirely satisfactory, and it is therefore evident that higher percentages than 2 per cent. should be available.

It is impossible to lay down any guide to a maximum percentage for all individuals for the induction of anæsthesia, as the range of individual differences is too great. In my personal experience 2 per cent. suffices for a small minority, 2·5 per cent. to 3 per cent. suffices for a good number, but 3·5 per cent. is required not infrequently, and a maximum of 4 per cent. is essential for exceptional individuals, and an inhaler should be capable of supplying this latter amount in order to meet all emergencies.

The Quantity of Chloroform used in inducing Anæsthesia.—There do not appear to be any definite records of the amount of chloroform used in inducing anæsthesia, but a rough estimate may be arrived at from a consideration of percentages administered. The following estimates are made from notes of cases in which the percentages of vapour (from Levy's inhaler) were noted, and the duration of each change of percentage was recorded. The calculation is made on the basis of an average of twenty respirations per minute, and an average intake of 500 c.c. per inspiration.

(1) Small female patient, aged 44. Time of induction, 10 min. 35 sec. Maximum percentage = 2 per cent. Total chloroform inhaled = 1,840 c.c. vapour, = 6·1 c.c. liquid chloroform, = ʒi ♏42.

(2) Adult female. Time of induction, 10 min. Maximum percentage = 2·5 per cent. Total chloroform inhaled = ·1,500 c.c. vapour, = 5 c.c. fluid chloroform, = ʒi ♏24. (Patient only slightly anæsthetized.)

(3) Male, aged 24, weight 13 stone. Time of induction, 6 min. 15 sec. Maximum percentage 3·5 per cent. Total chloroform inhaled = 1,137 c.c. vapour, = 3·8 c.c. fluid chloroform, = ʒi ♏4. (The respiration rate was high throughout the induction, so probably the estimate of the amount inhaled is too low.)

(4) Adult male. Time of induction 7 min. Maximum percentage = 4 per cent. Total chloroform inhaled = 1,433 c.c. vapour, = 4·8 c.c. liquid chloroform, = ʒi ♏20. (The respiration

rate was noted to be 32 per minute towards end of induction.)

(5) Male, aged 40, weight = 11 st. 10 lb. Maximum percentage = 3·8 per cent. Time of induction = 10 min. Total chloroform inhaled = 2,235 c.c. vapour, = 7·4 c.c. liquid chloroform, = 3ii ♏5.

(6) Female, average-sized adult, very anæmic from repeated hæmorrhages—an exceptionally susceptible subject. Time of induction = 4 min. 45 sec. Maximum percentage = 2 per cent. Total chloroform inhaled = 1,080 c.c. vapour, = 3·6 c.c. liquid chloroform, = 3i.

In this case the respirations were exceptionally free, and for the most part at a rate of 42 per minute; the calculation has therefore in this case been made on a basis of an average of 30 respirations per minute.

From such calculations as the foregoing it may be judged that from 1 to 2 dr. of chloroform must be inhaled in order to induce surgical anæsthesia in normal cases; larger quantities are, however, required when the vapour is not sufficiently concentrated, and the induction therefore unduly prolonged. Thus in one instance 12·5 c.c. (= 3iiiss.) of liquid chloroform were used over a period of twenty minutes without producing proper surgical anæsthesia, the percentage not having exceeded 2 per cent.

The amount of chloroform inhaled is practically the same as the amount actually evaporated when a valved suction inhaler is used, but a considerable excess of chloroform, beyond that actually inhaled, is evaporated when using a fabric or "ad plenum" inhaler.

The Percentage of Chloroform requisite to maintain Anæsthesia.—The highest percentage found necessary to induce anæsthesia in any one case is generally sufficient to maintain it, and when the former has been high, e.g., 4 per cent., more than sufficient. No definite rule can be laid down, as much depends upon the class of operation, but provided the patient has been fully anæsthetized, and no intermission of the chloroform has been allowed, and there is no suspicion of a muscular reflex on performing the initial incision, then it is generally necessary to maintain that percentage for a period varying from five up to fifteen minutes, and thereafter

gradually to reduce it. The strength of the vapour must be regulated entirely according to clinical requirement, and whereas 2 per cent. is frequently sufficient for all purposes, 3 per cent. and rarely more, is requisite under exceptional circumstances. In the later stages of a prolonged operation 1·5 to 1 per cent. is sufficient. It is doubtful if it is safe to use less than 1 per cent. except in cases of prolonged and severe operations. Alcock, as a result of fifty administrations with his form of "ad plenum" inhaler, concluded that 2 per cent. is generally required up to the twentieth to twenty-fifth minute, and 1·5 per cent. up to the forty-fifth, but these are average figures only.

The Individual Reaction to Chloroform.—Observations with percentage inhalers have placed the different susceptibility of individuals to chloroform beyond doubt. It is not easy to decide how this variability comes about, but a number of factors appear to be involved. The well recognized insusceptibility of alcoholic persons to the influence of anæsthetics may be fairly attributed to an abnormal resistance of the central nervous system. In some instances no doubt the central nervous resistance is subnormal, and this may have a pathological cause, as in the case of a fat, heavily-built man who had a small percentage of sugar in his urine, and who was fully anæsthetized in six minutes with a maximum of 1·8 per cent. chloroform. It is evident that subjects of large bulk must, other things being equal, require more chloroform to bring the blood to an anæsthetizing tension than small people, but it may not involve a marked difference in the time of administration, for a big person may have bigger lungs with a larger area of absorption, effecting a more rapid supply of vapour to the blood and tissues. Young children, and women as a class, are more susceptible than men, and this fact cannot be attributed entirely to the difference in bulk, for the converse of the above reason; it is notable, however, that circulation and respiration are more active in children than in adults. Where bulk is in abnormal

excess from an accumulation of tissue, as in the case of great muscular development, no doubt it has a determining effect, for muscular patients are "difficult" subjects. Fat people likewise are accredited with taking much chloroform, but this is by no means a regular rule, although it is known that fat absorbs a relatively large quantity of chloroform. The quantity of the blood, which may be depleted by hæmorrhage, and its content of hæmoglobin, are no doubt factors of importance. There are evidently many points to be taken into consideration, but it must be remembered that the main determining factor of the rapidity of induction in the normal individual is the rate of lung ventilation, and this may even obscure all other factors, when it is abnormal, either in deficiency or excess.

The "Body Dose" of Chloroform.—The chloroform content in the blood of an anæsthetized animal is recorded below according to the observations of Nicloux and Buckmaster.

Chloroform in mgms. per 100 *c.c. of blood in dogs.*

	Nicloux [1]	Buckmaster and Gardner [3]
Beginning of anæsthesia ...	30 to 40 ...	—
At full anæsthesia	40 „ 50 ...	16 to 31
Lethal dose	60 „ 70 ...	61 „ 69

There is a considerable discrepancy in the two sets of estimates at "full anæsthesia," possibly owing partly to a difficulty in estimating critical signs of anæsthesia in animals, but probably also because in Buckmaster and Gardner's experiments the estimation was made in some instances at the moment of the *return* of the corneal reflex.

The "lethal" dose in the above experiments is the dose which causes cessation of the respiration, which must be smaller than that causing complete cessation of the heart-beat, because the respiration ceases before the heart-beat in cases of overdosage. Sherrington and Sowton [1] have found that a solution of 75 mgm. of chloroform in 100 c.c. of blood, when perfused through the mammalian heart reduced the ventricular beat 75 per cent. (mean of six observations); sometimes the beat

was practically abolished, but recovery was complete in all cases on stopping the chloroform, even after perfusion for five minutes.

It is a matter of some interest to know what may be the equivalent solution tension of chloroform which causes cessation of respiration. There is no exact determination of solution tension in whole blood (p. 7), but we know that 70 mg. of chloroform in 100 c.c. of serum at 40° C. have a solution tension of 15·2 mm., which is the same as that of a 2 per cent. vapour (Moore and Roaf). We further gather from Sherrington and Sowton's papers [1] that a solution in blood has only three-quarters the potency of a solution in serum, and it may be deduced therefore that when the vapour tension of blood is in equilibrium with 1·3 per cent. to 1·5 per cent. vapour pressure, the respiration ceases.

This is a roundabout way of arriving at a result, but it is probably a reasonably accurate result. We know from Paul Bert's observations (p. 16) that 1·6 per cent. vapour will kill a dog in three to four hours, and we may reasonably conclude that after this length of time the whole body, blood and tissues, have nearly reached an equilibrium of pressure with the inhaled vapour. The process of charging up the body is a slow one at this low pressure; with a higher pressure the presumed lethal tension of 1·5 per cent. is reached in a much shorter time, as may be gathered from the remainder of Bert's table.

The solid tissues of the body absorb chloroform in varying proportions according to their nature. The actual amounts found in a dog killed by an overdose of chloroform are given as follows by Nicloux [1]:—

Blood	70	mgm. of chloroform	per 100 gm.
Liver	50.5	,,	,,
Kidneys	46·5	,,	,,
Spleen	28·0	,,	,,
Muscle	21·5	,,	,,
Heart	41	,,	,,
Brain	55·5	,,	,,
Bulb	85·0	,,	,,
Spinal cord ...	83·0	,,	,,

In fat, when very vascular, the chloroform content was found to be as high as 132 mgm.

From these data a rough estimate of the lethal dose, or overdose, of chloroform may be made by taking into account the relative proportions of the body tissues as stated in Vierordt's book, and in the case of a man of 63 kilos (about 10 stone) weight, reckoning blood as 4·9 per cent. of the body-weight (Haldane), I estimate the total chloroform absorbed in a lethal dose would amount to about 20 gm. (= $3\frac{3}{4}$ dr.).

It is evident that this estimate will vary roughly with the body-weight; for instance, in a child of 5 stone in weight the full lethal dose would be only 10 gm.

A. D. Waller [3] has made experimental estimations of the amount of chloroform absorbed into the body of animals in the process of overdosing them. His methods are evidently open to criticism, but the results are worthy of record. A cat weighing 2·9 kilos was killed in three minutes by 14·2 per cent. of chloroform, and it absorbed 0·63 gm.; a dog weighing 7 kilos was killed in three minutes by 13·2 per cent. chloroform and absorbed 2·615 gm. The equivalent weights to produce the same effect in a man of 63 kilos would be 13·5 and 23·0 gm. respectively.

Snow calculated that 36 minims (3·2 gm.) was a lethal body dose, but this allows for absorption by the serum of the blood and body fluids alone, leaving the solid tissues of the body out of account. The calculation is likewise based on a serious under-estimation of the total solubility of chloroform in serum, so that his calculation cannot be considered reliable.*

Vernon Harcourt [3] has estimated that 11·5 gm. of chloroform were retained in the body of a man anæsthetized under operation for sixty-two minutes with a maximum vapour strength of 2 per cent., reduced to 1 per cent. towards the termination, and

* Snow likewise erroneously assumed that the law of simple solubility of chloroform (as in water) applied also to serum from saturation downwards.

this estimate is quite in conformity with the estimation of 20 gm. for a complete overdose. The weight of the subject is not recorded. The details of this observation are given in the table on p. 72. There is reason to infer, however, that absorption of chloroform by the tissues from the blood is a relatively slow process, and it appears very probable that if the chloroform be administered rapidly, that is, in high concentration, the vapour tension may rise to a high point in the blood in advance of its value in the tissues, so that under such special circumstances the respirations may be extinguished by a dose which may be and probably often is lower than the estimate given above, viz., 20 gm. In other words, the blood and body fluids may be charged to the extent of 70 mgm. of chloroform, or thereabouts, per 100 c.c. of blood, whilst the much greater bulk of the body tissues are not yet charged to an equivalent vapour tension.

Estimations have been made by Waller [3] and by Brodie and Widdows of the amount of chloroform absorbed into animals within the induction period of anæsthesia. These figures may be translated into terms for a man of 63 kilos as follows :—

	Percentage of $CHCl_3$	Time of induction	Anæsthesia	Equivalent weight of chloroform absorbed
1	2·7	7 min. 40 sec.	Complete	5·0 gm.
2	3·1	4 „ 30 „	Complete	4·7 „
3	2·3	10 „ 0 „	Full ...	5·1 „
4	2·78	10 „ 0 „	Full ...	6·5 „
5	1·8	10 „ 0 „	Light	2·56 „

1 and 2, Waller.
3, 4 and 5, Brodie and Widdows.

The foregoing estimations of chloroform absorbed appear to be consistent with the estimations of the total quantity of chloroform which is inhaled to induce anæsthesia (p. 77), taking into consideration the respective conditions of administration, and the fact that only a part of the inhaled chloroform is absorbed.

In many records of fatalities under chloroform the

amount of the anæsthetic administered is reported, and the question has arisen, "Is such an amount capable of stopping the respiration from overdosage?"

The full lethal body overdose for a man of 10 stone weight would be about $3\frac{3}{4}$ fl. dr. (= 20 grm.). Let us halve this amount to avoid overstating the case. Half of $3\frac{3}{4}$ fl. dr. = 1 fl. dr. 52 minims, and in order that this amount should be absorbed about $3\frac{3}{4}$ fl. dr. should be administered in a valved inhaler, or nearly one fluid ounce on an open fabric mask. Taking these figures into consideration, and likewise the equivalent quantity required to induce ordinary anæsthesia, it does not appear possible that 1 fl. dr. or less administered can be capable of stopping the respiration under any circumstances; it may safely be concluded that in any case in which such a quantity is mentioned the patient did not die from overdosage. The concentration in which the chloroform is given is immaterial when the total quantity is insufficient to constitute a lethal body dose.

The Chloroform Content of the Blood in Human Fatalities.—The estimations on p. 80 apply to the lethal dose in the blood of animals intentionally killed by overdosage with chloroform; the examination of the blood of human subjects who have died under chloroform divulges an entirely different state of affairs.

The late Dr. J. H. Wells examined the blood of nine individuals who died under chloroform. In six of these the chloroform was present in quantities which were too small to be estimated, only three positive results being obtained, which were as follows:—

Subject	Chloroform in blood in mg. per 100 c.c
Child	2·37
Woman	3·98
Man	3·97

No doubt the method employed by Wells was not so reliable as those of Nicloux and of Gardner; his results

are consistently lower, the average of his observations on dogs' blood working out as follows :—

In full anæsthesia	...	...	16·08 mg. per 100 c.c.
At death...	...	...	20·91 „ „

The difference, however, between these averages and the results obtained at death in human subjects is remarkable. It is evident that none of these nine individuals could have died from overdosage.

CHAPTER X.

Death under Chloroform.

Liability.—The liability to death from chloroform is generally estimated at about 1 in 3,000 administrations, but it is probably considerably higher. In 13,393 administrations of chloroform annotated by the Anæsthetics Committee of the British Medical Association the number of deaths was eighteen. At least ten of these were directly due to the chloroform, yielding a mortality of 1 in 1,339. These statistics are especially interesting, being based on the reports of doctors who were accustomed to the administration of anæsthetics, so that deaths from gross negligence can be ruled out of account.

Numerical Incidence of Deaths per Annum.—The actual incidence of deaths from chloroform may be ascertained from the Registrar-General's Annual Report. In a proportion of the returns under the heading of "Death under an Anæsthetic" the nature of the anæsthetic is not stated, and in the following table the total number of deaths under chloroform has been calculated from the proportion of chloroform deaths in the total in which the anæsthetic was specified. All cases in which chloroform was used either alone or in combination or sequence are included in these figures.

Year	Total of all deaths under an anæsthetic	Relative proportion of chloroform cases per cent.	Calculated total of chloroform deaths
1919	292	72	210
1918	279	75	209
1917	280	84	235
1916	306	82	252
1915	261	82·5	215

Year	Total of all deaths under an anæsthetic	Relative proportion of chloroform cases per cent.	Calculated total of chloroform deaths
1914	300	75·5	227
1913	296	77·	228
1912	283	82	232
*1911	276	88	243
1910	234	83	194
1905	161	87	140
1900	116	90	104

* From 1911 onward a different system of compiling returns was instituted which might tend to increase the total.

Incidence in the Course of Administration.—Death under chloroform may occur at any stage of the administration, but in unequal distribution.

(1) The period of the greatest fatality is during the induction of anæsthesia and prior to or on the first commencement of the operation. The average of two series of available statistics would indicate that this period is responsible for about 85 per cent. of the fatalities, but it is possible that this figure represents a somewhat exaggerated view; thus Hewitt investigated 130 reports of chloroform deaths, and found that only fifty-four took place before operation or during some short or trivial operation, but this is an exceptionally low proportion, and is indeed at variance with his remaining statistics.

(2) The number of deaths occurring in the middle course of operations, following a satisfactory induction period, does not appear to be very considerable, but there are no data from which an exact percentage can be deduced.

(3) The mortality percentage again rises towards the end of, or after, the completion of the operation, and according to an analysis in Hewitt's book it is then as high as 16 per cent. How long after operation death occurred in these cases is not stated, but it is apparent that death at this period is coincident with the lightening of anæsthesia or very shortly after the total withdrawal of the anæsthetic and before the patient has been removed from the operating table—a remarkable fact to which too little attention has hitherto been paid.

Hewitt likewise gives the following instructive analysis of seventy-five cases, showing 91 per cent. of deaths to occur in the first fifteen minutes, the sudden drop thereafter being notable. The greatest incidence occurs during the period from six to fifteen minutes, which we may take to include the period of a prolonged induction.

Period of inhalation at which death occurred.

Under 1 minute	10
1-2 minutes	13
3-5 „	12
6-15 „	33
Over 15 minutes	7
Total	75

Etiology.—Strong and healthy individuals are more liable to this disaster than the asthenic. The Anæsthetics Committee of the British Medical Association found as follows :—

"In conditions of good health chloroform is very much more dangerous than other anæsthetics. In grave conditions chloroform still remains the least safe anæsthetic, but the disparity between it and other anæsthetics is far less marked than in health."

The Committee likewise found that chloroform is about twice as *dangerous* in males as in females. Hewitt's statistics show the disparity in sex incidence of *death* to be even more marked; they are as follows :—

Males	150
Females	59
Total	209

It is suggested in the Registrar-General's recent Reports that the larger number of operations for hernia and phimosis in male children may affect this disparity.

The precise relation of the age of the patient to liability to death has not been ascertained. The British Medical Association's Report shows the percentage incidence of cases of danger, including death, from

which it would appear that there is a somewhat greater liability to danger (including death) at an age over 30 years.

Status Lymphaticus.—Of recent years a condition of status lymphaticus* has been described in the post-mortem reports of some chloroform fatalities, but it cannot be said that the term has been employed in a precisely definite relation in these instances. The thymus has been generally enlarged, but not always so, and when the lymphoid tissue has been described as being in excess, it is not certain that it is so for a normal person, that is, a person who has not been affected by a wasting disease.†

The pathology of status lymphaticus is not clear. It is held that individuals suffering from this condition are liable to sudden syncope, and this appears to be a fact, apart from some confusion with death arising from suffocation by a large thymus in childhood.

It is certain that the majority of chloroform deaths are not associated with any such condition; thus in the Registrar-General's Report for 1916, in 164 deaths under chloroform or a mixture containing chloroform the condition of status lymphaticus was noted in twenty-two. It was found only once in death under other anæsthetics, so that it appears evident that the chloroform was the primary cause of death and not the condition of status lymphaticus, whatever subsidiary part this may play when it co-exists.

The proportion of twenty two cases of status lymphaticus in 166 chloroform deaths certainly appears to be high even if we question the genuine character of some of the post-mortem diagnoses. At the same time it must be remembered that a large proportion of chloroform fatalities occur in relatively healthy persons, who form a distinct class from the diseased subjects

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* For the literature of, and a discussion on, this subject see a paper on "Lymphatism" by Bellamy Gardner.

† H. C. Cameron's remarks in this connection are of interest.

which generally provide post-mortem statistics, and observations upon the frequency of the survival of the thymus and the existence of an abundance of lymphoid tissue in healthy persons should be available before positive conclusions can be drawn.

There is nothing in the clinical symptoms to distinguish a chloroform death associated with status lymphaticus from one not so associated, so that we may presume that if a persistent thymus is correlated with a tendency to sudden cardiac stoppage, the mechanism of its production is the same as that of fatal chloroform syncope; that is to say, that when status lymphaticus exists it may possibly render the subject more susceptible than ordinary to the mechanism of death under chloroform.

The Cause of Death under Chloroform.—The causation of death under chloroform has been the subject of a vast amount of experimental research and speculation of which a full account would occupy a volume in itself. Recent researches have, however, thrown a new light on the matter, and render it unnecessary to sift and discuss old theories in detail.

Overdosage with Chloroform.—Ever since the introduction of chloroform as an anæsthetic it has been patent that if it be given in sufficient quantity for a sufficient time the breathing is first depressed, and finally suppressed, and shortly afterwards the heart likewise stops.

The process of overdosage is a gradual one, and the onset of respiratory and circulatory depression is progressive. The complexion assumes a cyanotic tinge owing to the reduced pulmonary ventilation combined with deficient circulation, but an ashy grey tint follows when the circulation ceases. The pupils dilate progressively until they become widely dilated from an excess of the poison. The corneal reflex generally disappears at a comparatively early stage.

Overdosage never occurs suddenly. It has been held that rapidly charging the lungs with a high percentage

of vapour may produce sudden syncope from overdosage, but this theory has no experimental support. Sudden overdosage cannot be produced in this way experimentally. It is true experiments of this nature have been described (Snow, Lister, MacWilliam [2]), but they are subject to fallacy; the sudden administration of a high percentage to a *lightly anæsthetized,* or *partially recovered* subject will sometimes lead to sudden cardiac syncope, as also indeed will a moderate percentage, but the mechanism involved is fibrillation of the ventricles and not overdosage.

The Treatment of Overdosage.—Overdose is a common enough occurrence in the practice of inexperienced practitioners; it is a distressing condition, but it need not occasion acute alarm, for the appropriate remedial measures are simple and efficacious. The body should be inclined head downwards, and artificial respiration by Sylvester's method promptly commenced; the tongue, which tends to fall back and occlude the pharynx, should be pulled forward, and the air should be heard to enter and leave the lungs. The effect of this treatment is generally rapidly manifested, the heart-beat recovers its force, the breathing becomes spontaneous, and the natural colour of the face comes back again. In cases of severe overdosing, however, a minute or two of this treatment may be necessary. In Levy's and Rood's series of experiments on cats before referred to (p. 17) an attempt was made to estimate how far the process of overdosage might be carried with a prospect of recovery. In every case the overdosage was drastic; it was continued throughout the stage when single small breaths were drawn at intervals of ten or fifteen seconds and the breathing had ceased in the clinical sense, and a further period of from thirty seconds or longer was allowed to elapse after the final faint inspiration before artificial respiration was commenced. Under such conditions sixteen out of nineteen cats were restored, generally within the first minute after commencing artificial respiration. In two instances as

long as two and a half minutes and two minutes ten seconds of artificial respiration was required, respectively, and in one instance six minutes elapsed before natural respiration was resumed.

The details of one fatal case are as follows:—

hr.	min.	sec.	Percentage of chloroform	Remarks
3	0	30	2	—
3	2	30	7	—
3	13	30	7	Regular breathing ceased
3	13	35	7	One breath
3	13	45	7	,,
3	14	0	7	,,
3	14	5	7	Regular breathing recommenced, spasmodic but deep. Heart beat not palpable through chest wall, but a normal beat was recorded on the galvanometer
3	15	30	7	Breathing irregular
3	16	0	7	Breathing ceases. Heart beat still not palpable
3	16	30	—	No respiration since last note. Artificial respiration commenced; a difficulty found in maintaining a free airway; a little mucus removed from throat, but this did not cause much improvement. Artificial respiration continued for 15 minutes when there had been no attempt at spontaneous respiration, and the electric variations of the heart had died out entirely.

In the two remaining animals that could not be restored, owing to the preoccupation with the electric recording apparatus the exact moment of the cessation of respiration was not noted, but the interval before artificial respiration was started was probably about one minute thirty seconds in one case and about two minutes in the other.

These three fatal experiments show that if clear indications of failing respirations are disregarded, and if artificial respiration is too long delayed, then it may be impossible to revive the subject by artificial respiration alone.

The conclusions of the First Hyderabad Commission in respect of the efficacy of artificial respiration were as follows: The respiration was restored in every case in which artificial respiration was begun before the failure of the pulse. In forty-six experiments artificial respiration was delayed until immediately after the failure of the pulse,* and twenty-nine of these were successful. Every case was unsuccessful in which artificial respiration was delayed until cessation of the heart's beat. The pulse returned after artificial respiration was begun in mean, maximum, and minimum times of two minutes twelve seconds, six minutes ten seconds, and ten seconds respectively. The conclusions of the Second Report were that artificial respiration was in nearly every case (out of eighty-six dogs and thirty-nine monkeys) successful when artificial respiration was begun within thirty seconds of complete respiratory failure, very seldom successful in the period thirty to sixty seconds, and always unsuccessful after sixty seconds.

The *rationale* of the success of artificial respiration in overdosage appears to be as follows: On cessation of respiration the heart still beats but with decreased force, largely owing to excess of chloroform, but partly from deficiency of oxygen; its action is further decreased and finally extinguished by continued asphyxia. The main requisite of the heart is oxygen, and this is supplied by artificial respiration; even if the radial pulse has ceased to be palpable, the pulmonary and coronary circulations may be sufficiently active for revival of the heart (see p. 35). Excess of chloroform is rapidly thrown off into the pure air of the lungs as soon as a natural circulation is established, and the respiratory centre resumes activity; no doubt a rise in blood-pressure is an accessory factor in restoring the respiration. If the heart-beat is entirely extinguished before

* This appears to refer to the crural pulse, which would be expected to disappear later than the radial pulse.

artificial respiration is begun the latter must obviously be useless.

When the heart has ceased beating nothing will restore it except massage combined with artificial respiration, and this should be always successful. Adrenalin in my experience has no beneficial effect upon a heart overdosed to the extinction of its function.

Clinical Evidence of Death by Overdose.—Do deaths actually occur in this way in clinical practice? The possibility is always present in the event of carelessness on the part of the administrator, but it is hardly conceivable that human subjects are ever treated with the deliberate neglect of Levy and Rood's experimental methods. It is remarkable that out of the whole accumulation of reports of death under chloroform I have not been able to find a single one which undoubtedly bears this interpretation, and this in face of the prevalent view that all deaths under chloroform are due to this cause.

J. Snow carefully observed the sequence of events in overdosed animals. He came to the conclusion that death never happens in man from overdosing with ordinary percentages of chloroform, for it occurs in another fashion, the heart stopping suddenly before the breathing is affected. He claimed, however, that the heart could be suddenly overdosed by from 10 per cent. to 12 per cent. of vapour, and performed some experiments which he considered demonstrated this fact. It is certain that in this latter point he was in error,* for high percentages of chloroform if administered continuously are incapable of producing a sudden stoppage of the heart, but will cause an overdose in precisely the same way as lower percentages, only in a shorter time.†

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* See p. 91 for an explanation of this false conclusion, also Levy [1], p. 373.

† If Snow's theory were correct, it would be immaterial, for percentages of 10 or 12 per cent. are quite outside the range of vapours obtainable by ordinary appliances, as is seen from the estimations recorded in Chapter XI.

Levy [5] re-examined the collection of cases of death published by the Anæsthetics Committee of the Royal Medico-Chirurgical Society, ninety-eight cases in all; he found that in 87 per cent. deaths could not have been caused from overdose. Of the remaining cases, in six overdosage appeared improbable, and no opinion could be expressed upon the remaining seven. In the whole ninety-eight reports, however, *there is not a single one which contains definite evidence that the patient died of overdosage.*

"**Chloroform Syncope.**"—If death under chloroform is not generally caused by overdosage, how then is it to be accounted for? Dastre, Embley, Yandell Henderson, L. Hill [1], A Wilson and Robert Kirk have all sought to advance explanations in accordance with clinical facts, and their work has been examined in former chapters. Of these Kirk urged the thesis that death occurred only during light anæsthesia, and made the important observation that the heart was liable to become irregular and intermittent on stopping the administration of chloroform; Yandell Henderson has likewise insisted on the association of death with pre-existing light anæsthesia.

There can now be no doubt that these deaths are in fact conditioned by light anæsthesia. In the series of reports analysed by Levy [5], there was definite clinical evidence that 62 per cent. of the patients were lightly anæsthetized at the moment of death; that is to say, some sign of recurring consciousness or a semi-conscious state was explicitly mentioned.

In a majority of clinical reports also it is evident that death occurred from primary heart failure. It has been seen that Snow made a sweeping assertion on this point, and he had many very carefully reported cases upon which to base an opinion. It must be admitted, however, that many clinical reports do not portray any definite syndrome of symptoms at the moment of death, as is natural in the event of such a sudden and disconcerting catastrophe. The actual cause of death

has been deduced from work which is mainly experimental.

In 1911 Levy [10] communicated a note to the Physiological Society describing a hitherto unrecognized form of sudden cardiac failure which occurred in cats under chloroform, and stating that he had, acting on a suggestion made by Prof. Cushny, looked for and found ventricular fibrillation in such cases. At the same time he showed that an exactly similar form of death could be reproduced by injecting small doses of adrenalin into the vein of a cat lightly anæsthetized with chloroform. These observations became the starting point of a series of experiments elucidating the conditions under which ventricular fibrillation occurs, and showing that it happens only in light chloroform anæsthesia, never in full or deep anæsthesia,

These observations have been summarized in Chapter IV, and they provide an explanation of sudden cardiac failure as it occurs at any stage of the administration of chloroform, and in fact the only wholly acceptable explanation. The acceptance of this view involves the corollary that all clinical deaths occur under light anæsthesia, and it is upon these experimental data that the claim is mainly based.

MacWilliam [2] had previously noted the incidence of ventricular fibrillation in the cat's heart under chloroform, and considered that the occurrence of fibrillar contractions might be a cause of death "in some abnormal conditions where the ventricles became prone to this disastrous form of activity"; but he at the time saw no proof that such a mode of cardiac failure might result from the administration of chloroform in the ordinary way to healthy animals. However, MacWilliam's [1] subsequent experience of many years' duration led him to other conclusions, which are practically in agreement with my own. His final views are contained in a paper published in 1914; he does not consider that there is any other hypothesis of early chloroform death in man that stands on any secure foundation.

A remarkable confirmation of the stage of anæsthesia in which the chloroform death occurs is found in the extremely low chloroform content of blood in fatal cases; the results of the investigation by Wells already referred to (p. 84) was entirely unexpected by this observer, and inexplicable on the current theories of death at the time.

It has been suggested to me that the term "chloroform syncope" should be restricted to the sudden cardiac failure from ventricular fibrillation; this form of syncope presents certain clinical features which serve to distinguish it from the condition due to overdosage.

The Clinical Manifestations of Ventricular Fibrillation.—This form of syncope is extremely sudden in onset, and the patient is plunged from life into death in an instant. There is one preceding sign of danger which must invariably be present, but which is rarely actually observed. The pulse is accelerated, and at the same time becomes irregular; the irregularity may in some intsances be difficult to follow, but it is frequently well pronounced, and the short pauses convey a flickering impression to the finger on the pulse. The heart-beat then ceases absolutely suddenly, the face is blanched white, the pupils dilate extremely, and drops of sweat may form on the face and body.

The respiratory phenomena following ventricular fibrillation require careful remark; they are simple and distinctive. The respiratory centre is never strongly depressed by the chloroform at the moment of syncope, and therefore the respirations continue until the centre fails from want of blood. Generally there are a few respirations only, and these may take the form of deep gasps, because the centre is at first stimulated by the sudden anæmia and consequent want of oxygen; but whether or no the respirations are exaggerated depends upon the precise degree of anæsthesia. There may, however, be a persistent tendency towards recovery of the respiration, often continuing long after the heart has ceased to beat, and should the heart recover, the

breathing is immediately resumed. A second cardiac syncope, with its attendant gasping respiration may in some circumstances supervene on such a recovery, and thus there may occasionally arise considerable confusion in the clinical interpretation of the true order of events.

Sudden anæmia likewise excites the spinal motor nerve centres of the skeletal muscles;* some evidence of muscular convulsion is therefore generally observed, and in very lightly anæsthetized subjects this may be a pronounced feature of death by ventricular fibrillation. An extreme tonic contraction of the whole of the body muscles, accompanied by opisthotonus, is sometimes described in man; it is frequently observed in very lightly anæsthetized cats. The "epileptiform fit," which has been in some cases described as preceding death, is in all probability an asphyxial convulsion succeeding syncope.

To a certain extent broad clinical distinctions have been drawn between syncope from ventricular fibrillation and the condition of overdosage, and recognized in certain brief expressions. Thus it has been said that a "white syncope" is fatal, but that a "blue syncope" is not fatal. Again, that when the heart fails before the respiration the syncope is fatal, but when the respiration fails first, the patient recovers. Both of these expressions of distinctions are to a certain extent correct, and in so far as it is possible to make careful observation, the majority of cases are found to conform to one or other of these two classes. However, certain qualifications must be pointed out: for instance, in such cases in which a fortuitous asphyxial condition from obstruction of the air passages precedes a primary cardiac syncope, then the expected pallor may be obscured by a cyanotic tinge; again, the cardiac syncope is not by any means always fatal.

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* Kussmaul and Tenner hold that muscular convulsions arise mainly from anæmia of the parts of the brain posterior to the optic thalamus.

The conditions under which ventricular fibrillation occurs during the administration of chloroform in man are in accordance with the theoretical considerations in Chap. IV, and may be summarized as follows :—

(1) During struggling or excitement.

(2) On the cessation of the administration, temporary or permanent.

(3) On abrupt re-administration of chloroform, after partial recovery from anæsthesia.

(4) By strong sensory stimulation (some operative procedure) under light anæsthesia.

(5) Some combination of the foregoing conditions.

(6) Following the injection of adrenalin for surgical purposes under light anæsthesia, or in order to combat shock after the total withdrawal of chloroform.

(7) Following recovery from an asphyxial condition.

Some of the varying conditions of primary cardiac syncope under chloroform are exemplified by the following abstracts of reported cases :—

(1) *Death following the Injection of Adrenalin.*—The patient was a male, aged 26, a well-developed and healthy man. Operation for deflected nasal septum. Anæsthesia was induced by chloroform given upon a Skinner's mask, and it was decided to inject some adrenalin (5 minims of a 1 in 1,000 solution) into the nose subcutaneously. At the time of the injection anæsthesia was light (a brisk corneal reflex being obtainable), the pulse was very strong and the patient's colour good. No more chloroform was given. About one minute after the injection the pulse suddenly became very rapid and then imperceptible; at the same time the patient's colour became leaden grey and the pupils widely dilated. About three deep gasps were taken after the pulse had failed and then respiration ceased. Appropriate remedies failed to restore the patient. At the post-mortem examination nothing abnormal was found in any of the organs. (Dupree.)

(2) *During Struggling.*—The patient was an agricultural labourer who had never had an illness or an operation before. He was admitted for hæmorrhoids. He was given the usual preparation, but not morphine and scopolamine. The urine had no albumen. He was a stolid taciturn individual. He breathed well and quietly when I commenced the anæsthetic and was rather pale in complexion with large pupils. I had given about

5ii of $CHCl_3$ when the excitement stage commenced. He fell off the table and sat upright on the floor. He had pulled the mask off his face by then. When he sat up on the floor he was rather red in the face and breathing shortly and in gasps. His eyes were open and I thought he was coming round. Then he collapsed slowly backwards. We lifted him on the table and he was beginning to get cyanosed then. He then breathed great gulps of air once or twice and then stopped. He was, of course, cyanosed then, but not remarkably so. We started artificial respiration and oxygen. We injected 1 c.c. of pituitrin. This was about 1 p.m. At 1.30 we took him into the theatre and opened the abdomen. The wound oozed slightly dark blood but did not bleed normally. The heart was massaged, artificial respiration and oxygen being given simultaneously until 2 p.m. when we decided it was no use continuing. During these operations he got a slightly better colour but not much. No obstruction was found in the trachea or larynx post-mortem, and the patient did not have a high palate or exhibit any tendency to swallow his tongue or secrete an excess of mucus. The lungs were quite normal. (Private communication.)

Note on above case.—Cyanosis, preceded by a phase of simple congestion is sometimes remarkd in cases of syncope following struggling. It is no doubt largely due to the filling of the veins from the intense muscular rigidity of semi-conscious struggling, and partly to spasm of the respiratory muscles; it naturally masks the potential pallor from sudden depletion of the arteries.

(3) *Re-application of Chloroform.*—The patient, a man, 30 years of age, was affected with hydrocele. The chloroform was poured on a little cotton which was placed at the small end of a cone, into which the folded towel made use of was rolled. About a drachm and a half was first poured on the cotton, and the patient was told to inhale in long and deep inspirations. This quantity being nearly evaporated in two or three minutes, a drachm more was added. After a few inspirations rigidity and struggling came on; these subsided, but in a little time returned more strongly than before, and the towel was removed from the face until the struggling ceased. The patient, however, not being sufficiently insensible to undergo the operation with the necessary quietness, the towel was reapplied, when, after a few inspirations, the pulse suddenly ceased. The face and the whole surface of the body turned pale, the eyes rolled upwards and inwards and the breathing become very slow, but full and deep, the intervals between the inspirations becoming longer, until the respirations ceased altogether. The patient died before the

operation was begun, and within five minutes from the commencement of inhalation. During the application of various means of resuscitation, the breathing returned and continued for the space of three or four minutes, but the pulse and sounds of the heart did not return. (Snow's "Anæsthetics.")

(4) *Death from Sensory Reflex.*—The patient, a girl of 15 years of age, was operated on for genu valgum by Macewen's method. Chloroform was given on lint; she took it well, the operation was performed and the splint in process of being put on. At this stage, under the impression that all painful operative procedures were completed, the anæsthetic was discontinued. The patient was then breathing quietly; she had a good pulse and normal colour; the pupils were slightly contracted and the corneal reflex was present—in fact, she was coming out of the anæsthetic, but was sufficiently insensible to bear ordinary manipulations or even incisions without feeling pain, and was as well as anyone could wish her to be. At this instant the surgeon suddenly forcibly flexed the left knee, which was stiff owing to the osteotomy having being performed on that side a few weeks previously. The adhesions gave way with a crunching sound, and the patient uttered a scarcely articulate cry, immediately became deadly pale, and began to breathe deeply. She passed at once into the following condition: the head was turned to one side, the face was deadly pale, the eyes were slightly open, the pupils were widely dilated and she was taking deep inspirations, the air passing freely into the chest; the muscles of the alæ nasi were also acting, and the pulse was imperceptible at the wrist. The symptoms conveyed the impression that she had fainted. To drop the head, elevate the limbs, and apply hot sponges, was the work of a moment. She continued to make strong respiratory efforts, and air was freely entering the lungs but there was still no sign of the radial pulse. It appeared at first that the patient would probably recover—it seemed impossible that she could die with such active respiration; but the breathing, without shading off in the least, suddenly ceased, and every effort to restore life failed. (Alex. Wilson.)

(5) *Death after Operation, the Chloroform being withdrawn.*—A boy, aged 15 years, had been anæsthetized with chloroform for the removal of post-nasal adenoids. The operation had been completed and the anæsthetic withdrawn, when the patient was noticed to be breathing deeply. The operator observed some peculiarity about the colour of the face, but was reassured by the presence of free respiration. The respirations, however, suddenly ceased, and all efforts to resuscitate the patient failed. (A. Wilson.)

Death under Chloroform-ether Mixtures.—When chloroform is given in conjunction or in sequence with other anæsthetics, such as ether, the symptoms occurring at death may be somewhat obscured or confused. The chloroform effect *per se* upon the heart may be light but the ether effect fairly pronounced, so that the total general anæsthetic effect may appear well developed, and death under such circumstances may appear a most mysterious circumstance.

In recent years mixtures of chloroform and ether have been extensively employed with the idea of retaining some of the advantages of chloroform, and at the same time obtaining full anæsthesia with less risk of overdosage. No doubt the risk of syncope from overdosage is in this way reduced, but a large number of fatalities result from the use of this mixture, and the number is increasing with its more extended use. The figures given by the Registrar-General are eloquent upon this point—the proportion of deaths under pure chloroform are becoming reduced, whilst those under chloroform and ether mixtures are becoming increased, the total deaths under chloroform and its mixtures being fairly constant. At the same time the deaths under A.C.E. mixtures have fallen off.

(The following figures do *not* include a proportion of the deaths with "anæsthetic not stated.")

Year	Pure chloroform	C. E. Mixture	A. C. E.
1919	88	56	4
1918	81	46	5
1917	106	45	6
1916	112	39	8
1915	109	24	6
1914	111	28	7
1913	110	25	7
1912	117	24	7
1911	142	33	11
1910	119	20	—
1909	108	18	—
1908	108	4	—
1907	99	5	—

It must be remarked likewise that ether is a cardiac stimulant, and if given *subsequently* to chloroform it

may assist the onset of ventricular fibrillation as the effect of chloroform wears off. The principle of inducing anæsthesia by chloroform or chloroform and ether and following it up by open ether is thus entirely wrong; it arises from an inability to induce anæsthesia by ether alone in the open method sufficiently rapidly, and unfortunately there has been a tendency to an increase in the employment of this sequence with corresponding fatal results. The figures given in the Registrar-General's reports are as follows:—

Number of deaths in which it is stated that chloroform or chloroform and ether was followed by ether.

1913	1914	1915	1916	1917	1918	1919
Nil	Nil	1	2	4	8	9

Note.—These figures do not allow for a corresponding proportion of the deaths with "anæsthetic not stated."

J. McCardie maintains that the effect of adrenalin injections in nasal cases under chloroform-ether mixtures is more pronounced in moderately full anæsthesia, and not observed under extremely light anæsthesia; this may be so in some cases, as the heart may be affected in too slight a degree by the chloroform in the mixture to become irritable despite definite symptoms of anæsthesia, as can be shown by experiment,* but it would not appear possible so to adjust the anæsthetic with any certainty of safety to the patient.

Prevention of Death under Chloroform.—For many years past the attempt has been made to prevent death under chloroform by the restriction of the percentage administered, on the theory that death is caused by overdose alone. This teaching has failed to decrease the incidence of death, which has indeed tended to increase rather than otherwise.

The study of the cause and conditions of death by ventricular fibrillation under chloroform has revealed the essential principles of the safe administration of chloroform to be:—

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* Levy [14].

(1) *To maintain a full degree of anæsthesia.*

(2) *To make the administration continuous.*

These principles will be amplified in considering the clinical procedure of the administration.

Spontaneous Recovery from Chloroform Syncope.—A brief reference has already been made to spontaneous recovery from ventricular fibrillation in man (p. 31), and in my opinion this is a far more common event than is generally supposed (Levy [16]). Three cases of sudden cardiac syncope have been reported by Seymour Jones following the submucous injection of adrenalin under chloroform; these were certainly due to ventricular fibrillation, yet they all recovered without treatment. Further, a number of reports of recovery from primary cardiac syncope in chloroform anæsthesia are recorded in the Report of the Anæsthetics Committee of the British Medical Association, and in these instances there can be little doubt that fibrillation had occurred. Such recovery can, however, only occur within a very brief period; when the cardiac muscle has become asphyxiated it cannot pick up the normal beat, and two minutes may be regarded as the maximum period within which such recovery may be expected. There are no measures known to facilitate spontaneous recovery; artificial respiration promotes a small degree of circulation, so that the intense pallor is succeeded by a faint pinkish tinge; but it does not appear to have any beneficial influence upon fibrillation.

The patient should always be given a chance of spontaneous recovery, but after the lapse of two minutes resort should be had to cardiac massage with as much expedition as possible.

Treatment of Syncope from Primary Cardiac Failure.—Cardiac massage is the only active treatment which will restore the fibrillating ventricles to a regular beat.* The function of massage is purely one of setting up an artificial circulation,† which is itself useless unless the

* Batelli was successful in the application of an electric current of high voltage, but this would not appear to be applicable in man.

† Levy [15 and 16].

blood be aerated; cardiac massage must therefore be supported by an artificial respiration.

The theory of the action of massage on the fibrillating ventricles is as follows: The human heart has a strong tendency to recover from ventricular fibrillation, but it cannot recover when once the heart has become asphyxiated from cessation of the circulation; by restoring the circulation the heart derives an extended opportunity of recovery. In cats the beat may be restored in practically every instance if massage be continued sufficiently long, the longest time in my experience being forty-eight minutes. The tendency to spontaneous recovery in man is apparently even stronger than in cats, so that there is every prospect of success in clinical cases, provided efficient measures be adopted.

The ventricles pass from fibrillation to a normal beat by a sudden transition, and the blood-pressure mounts up rapidly, and generally to a satisfactory height; occasionally, and especially after prolonged massage, the blood-pressure may be low, but this may be remedied by the injection of pituitrin, as it is largely a vasomotor affection, and once the blood-pressure is raised it remains up.

Occasionally the fibrillation ceases spontaneously whilst the heart is asphyxiated, and therefore unable to resume its beat; in such a case massage simply serves to remove the asphyxia and then the heart-beat returns very rapidly, but in a more gradual fashion as the asphyxia passes away.

The principles and the technique necessary for cardiac massage are clear. The heart must be efficiently grasped, the fingers must get right round the right ventricle, so that the contents of both chambers are expelled. An efficient compression may possibly be sometimes effected, especially in children, from below the diaphragm, but the only reliable method is to introduce the hand into the pleural cavity and grasp the heart outside the pericardium. This may be performed

according to the method described by Bost and Neve, who applied it with success in a case in which the subdiaphragmatic method had failed. The subdiaphragmatic method has been occasionally successful, but it has a vast number of failures to its discredit. Bost and Neve's method is to make an abdominal incision, and through this the attachment of the diaphragm to the left costal margin is cut for two inches. The left hand is inserted into the left pleural cavity and the heart grasped outside the pericardium. During massage the parts are pressed around the wrist to prevent air entering the pleural cavity.

The rate of compression of the heart does not appear to be a matter of great importance; it must be sufficiently rapid to maintain a measure of systemic blood-pressure, but it can hardly be wise to exceed the normal rate of the heart. Massage should not be abandoned until a period of an hour has been passed in its performance, for although recovery may occur quite rapidly, it may, on the other hand, be long delayed. Experimental experience demonstrates the benefit of intermitting the massage if recovery does not occur within the first ten minutes of continuous massage, and thereafter pauses should be allowed at intervals, these pauses varying from fifteen up to sixty minutes' in duration; recovery frequently occurs during a pause or immediately thereafter on the resumption of massage.

An efficient artificial respiration is an essential factor of sucess. In such a method as Bost and Neve's, the Sylvester method is not readily applied and is liable to suck air into the pleural cavity. Perflation of the lungs is much preferable, and makes certain of air entering the lungs. Mouth to mouth perflation may be performed in an emergency, but means should be available for performing intubation of the larynx; the perflation may be performed by human lung power, a pair of bellows, or an intermittent pump. A continuous stream of air from an intratracheal ether apparatus will serve if the pressure be not too high, or a stream of oxygen

direct from the cylinder should answer admirably if this be properly controlled.

The heart itself has remarkable powers of recovery, but it is hopeless to rely on this without proper aeration of the other tissues. When more than a few minutes have elapsed before massage is commenced the ultimate results are generally unsatisfactory, even if the heart-beat is restored, for nervous symptoms develop as a result of the prolonged oxygen starvation of the nerve centres. The patient presents features of severe cerebral irritation, with rigidity, screaming, tetany, and incontinence of urine and fæces, which generally but not invariably terminate in death.

In the interest of the patient, therefore, cardiac massage should be in active operation in not less than five minutes from the moment of syncope. There is, however, a good prospect of success if this interval be unavoidably exceeded, and in one recorded case recovery ensued after as long an interval as thirteen minutes, but the patient took fourteen days to recover (Mollison).

It is advisable partially to invert the patient during the performance of massage, as the flow of oxygenated blood to brain is thereby promoted.

One can hardly look for the same measure of success in human subjects as one obtains in the laboratory in cats; the same methods are not applicable. However, there can be little doubt that cardiac massage, properly performed, should be a very efficient means of restoring the normal beat to fibrillating ventricles in the human subject.

The following account illustrates the successful practice of cardiac massage.

Private, aged 22, was admitted to hospital suffering from a severe gunshot wound of the left hand; the wound was very septic.

As it was considered necessary to amputate the finger he was given a general anæsthetic—a mixture of chloroform (two parts) with ether (three parts), alternately with pure ether on an open gauze mask. He was taking the anæsthetic quite well and was wheeled from the anæsthetizing room into the operation theatre.

He was lifted on to the operating table when he suddenly became ghastly white, sweated profusely and the pupils became widely dilated. Breathing continued slow and regular but rather shallow. No pulse or cardiac impulse could be felt or heart sounds heard. An incision a little to the left of the middle line was rapidly made into the upper part of the abdomen, the right hand was inserted into the abdomen and a flabby mass, supposed to be the heart, seized through the diaphragm and energetically and rhythmically squeezed. In a short time the flabby mass suddenly became hard—like a cricket ball in the hand and firm and regular and slow contractions commenced. After a little these firm contractions became tremulous and threatened to cease, but on squeezing again became firm and regular; this routine was carried out several times and at last a regular heart beat and regular pulse were established. In about twenty minutes he was taken back to the ward, where a rectal saline injection was administered.

In the evening he suffered very considerable pain in the abdomen and chest which was allayed by hypodermic injections of morphine. He made a good recovery. (Sichel.)

Another good account of a successful case is contributed by V. B. Orr.

Cardiac Massage in Asphyxia and Overdosage.—The principles of cardiac massage for conditions other than ventricular fibrillation, such as neglected overdosage or asphyxia, are essentially similar. In my experimental experience, the heart, even when overdosed to extinction of beat, responds rapidly to massage if performed within the five minutes' time limit. After longer periods of inaction and consequent asphyxia, longer massage will be required. Gunn has pointed out the advantage of intermitting massage in the case of overdose; no doubt continued massage is deleterious, and an occasional short rest enables the heart to take up a stronger beat. The recovery from overdose or asphyxia is a gradual one; a feeble beat is at first elicited, and this becomes stronger as massage is continued, and further stronger when the heart-beat becomes purely automatic; that is, the ventricles recover gradually as they receive oxygenated blood, and as the blood throws off an excess of chloroform through the lungs.

CHAPTER XI.

The Administration of Chloroform. The Physical Principles of Methods and Apparatus.

The administration of chloroform consists essentially in causing the patient to inhale chloroform vapour in concentrations suitable to his requirements, and in the performance of this task lies the foundations of a successful administration. The critical function, therefore, of most methods is the evaporation of chloroform in a correct amount; this is a matter of considerable delicacy on account of the number of physical conditions involved, the small proportion of vapour which is required, and the reaction of the subject to small variations.

Physical Factors affecting Evaporation.—A consideration of evaporation from a physical standpoint and under varying circumstances is an essential preliminary to the description of the various forms of chloroform inhalers.

(1) *Temperature.*—The evolution of vapour is profoundly affected by the temperature at which the evaporation is conducted, as is seen in the vapour saturation table given on p. 3; under conditions of partial saturation, the amount of vapour taken up is affected by changes in temperature in the same ratio as if the vapour were saturated, for example, thus:—

Table I.

Chloroform at a constant temperature of	Percentage of vapour yielded under conditions of one tenth saturation Per cent.
40° F.	1·0
50° „	1·3
60° „	1·7
70° „	2·2
80° „	2·8
90° „	3·5

Note.—This table is based on the assumption that the air comes to the same temperature as the chloroform with which it comes in contact.

In the course of evaporation the temperature of the liquid chloroform falls progressively from the abstraction of latent heat. When small quantities of chloroform (0·5 to 2 c.c.) are exposed to a draught of air on an absorbent fabric, the temperature falls rapidly to 0° C., or 2 or 3 degrees lower, but when the currents of air emanate from direct respiration the warmth of the expired air provides a degree of compensation, and the temperature of the chloroform only falls to about 5° C. Even thus the percentage of vapour diminishes considerably from decrease of temperature, but provided that a small quantity only (say 5 to 10 drops) of chloroform is exposed to the small number of respirations which just suffice to evaporate it completely, the fluctuation is not of moment, for the alveolar atmosphere will come to the mean of the descending scale of vapour tensions, and exert a mean anæsthetic effect which will be continued throughout successive repetitions of the procedure. The rule must be, therefore, in evaporating chloroform by direct respiration on a fabric mask, to apply only drops or small measured quantities of chloroform at definite intervals of a small number of respirations. With large douches on a fabric mask slow and long continued changes of temperature occur which will be capable of leading to definite changes in the anæsthetic effect upon the patient.*

When large masses of chloroform are submitted to evaporation, such as may be contained in an inhaler, some form of temperature regulator is essential; the usual form is a water-jacket, and as water possesses the highest specific heat of any substance, no other can be more suitable for this purpose.

(2) *The Velocity of the Air Currents.*—A fast current of air accelerates evaporation on the whole, but at the

* The foregoing and many subsequent particulars are abstracted from a paper by A. G. Levy [12]. W. L. Symes previously published a short paper on experiments conducted on somewhat similar lines.

same time takes up a less proportion of chloroform vapour per unit volume of air.

The following table shows the variation in the vapour evolved from chloroform in a Vernon Harcourt container, according to the rate of flow of the air current, all other conditions being maintained constant (Levy [9]).

TABLE II.

Maximum rate of draught in c.c. per second	385	320	190
Percentage of chloroform taken up	1·4	1·55	2·0

Further examples of variations in percentage from this cause are contained in Table III, p. 112.

In many methods of administration the vaporizing currents are produced by the act of respiration, and are hence a varying factor. The frequency and depth of inspirations considered individually have no direct bearing upon the rate of the air current; it is the rate of draught during the act of inspiration which has to be considered—this is the true rate of inspiration, colloquially expressed as *force* of inspiration. An account of its measurement has already been given on p. 54.

The varying force of inspiration is a considerable difficulty in the way of administering a constant vapour, but it may be mitigated by the use of special devices. For the moment it may be indicated that changes in slow currents produce less variation in percentage than similar changes in more rapid currents,* so that it is desirable to cause the currents to slow down as far as possible at the point of uptake of the vapour. If the air be drawn through a tube or aperture the velocity increases as the channel is constricted, and in the absence of a tube the velocity is greatest at the point of intake, i.e., at the oral or nasal margins.

(3) *The Air Space between the Chloroform and the Point of Intake.*—In the case of the air currents passing

* Levy [13].

over the fabric, the further the chloroform surface is removed from the point of intake the less chloroform is taken up.

The figures in Table III show the result of adjusting a vaporizing surface to various vertical measurements above a central air intake.

TABLE III.

Vertical measurement of air space	Velocity of air currents in c.c. per sec. at point of intake		
	550	360	160
4 cm.	0·85	1·0	0·9
3 ,, ...	1·85	2·4	2·4
2 ,, ...	1·75	3·1	3·6
1 ,, ...	1·60	2·7	4·75

The points of practical importance to be gathered from this table are (1) that slight alteration of distance of a fabric inhaler from the face will cause considerable variations in the percentage inhaled, and that it is impossible to rely on regulating the percentages, except in an extremely rough manner, by adjusting the air space within these small distances. (2) That the variations in percentage due to alterations in the force of breathing become negligible when the mask is held well away from the face (owing to the slowing down of the air current at a distance from the point of intake).

(4) *The Absorbent Quality of Fabrics.*—The spread of the chloroform in different fabrics varies a good deal. Thus equal quantities of chloroform dropped on single thicknesses of domette, lint and linen towel form patches of relative areas = 2·9, 1·8 and 1 respectively. The spread in the case of domette is not only larger, but is also more evenly distributed; lint is more spongy and tends to retain the chloroform at the point of application, the spread being distinctly less on the fluffy side.

The area of spread in a given material is found to be roughly proportional to the number of drops applied to a point of the fabric.*

* The spread of chloroform on fabrics may be studied by dissolving a small quantity of Ehrlich's "Dahlia" dye in the chloroform.

(5) *The Texture of Fabrics.*—The amount of chloroform evolved by a fabric is considerably affected by the degree of fineness of its texture. The coarser the texture the more air will pass through its meshes and so come in close contact with the chloroform. The following observations were made on equal surfaces (200 sq. cm.) of three materials so arranged that the air current could pass either entirely over, or partly over and partly through them according to their texture.

TABLE IV.

Linen towel Per cent.			Fine flannel Per cent.			Domette Per cent.
1·7	...	...	3·4	...	...	4·3

It is thus evident that inspiration "through" a fabric yields a higher percentage than inhalation "over" the surface.

Breathing through or "perhalation," is encouraged according as the edges of the mask upon which the fabric is stretched approach the face and discourage the entry of air under them. An incurving of the edges, as in the ordinary Skinner pattern, will also tend to divert a portion of the air through the fabric if it be of an open woven character.

(6) *The Area of the Surface of Evaporation.*—Evaporation is generally stated to be proportional to the area exposed. Although this is probably true for very large surfaces exposed to atmospheric conditions, it does not apply generally to the special circumstances of the inhalation of vapour from an open surface. The relation of area to vapour percentage was ascertained by drawing an air current over a circular area of chloroform in a direction from the periphery to the centre (as would be also approximately the case in inhaling from a towel or some such fabric held over the mouth), and percentages of vapour found to be evolved from different-sized areas are shown in the following table.

TABLE V.

Area of circular patch of chloroform	Percentage of vapour obtained	Percentages calculated in proportion to diameters	Percentages calculated in proportion to area
200 sq. cm.	3·35	3·35	3·35
70 „	2·0	2·0	1·17
50 „	1·6	1·6	0·34
25 „	1·2	1·15	0·42

The vapour evolved is seen to be proportional to the diameters of the areas, or what is the same thing, the peripheries of the circles, and not to the superficial areas. The explanation probably is that a great part of the chloroform is absorbed at the first contact with the chloroform at the periphery of area, where the current is slowest.

The foregoing results apply to a draught of air passing *over* a surface only. When the air is made to pass entirely *through* an area of open wove fabric, such as domette, only partly wetted with chloroform, then the percentage of vapour taken up is found to vary approximately with the proportion of the fabric which is so wetted, that is, according to the proportion of air which comes in contact with the chloroform.*

TABLE VI.

Percentages obtained by aspiration through domette.

Proportion of domette bearing chloroform	Percentage obtained	Percentages calculated in ratio of areas employed
One fifteenth	0·32	0·3
Two fifteenths	0·65	0·6
Four „	1·20	1·2
Eight „	2·35	2·4
Twelve „	3·5	3·6
Fifteen „	4·3	4·5

It is evident from the foregoing table that the device of breathing through a fabric offers very valuable facilities for regulating the evolution of vapour by

* The percentages in these tables were obtained with a current of air passing in one direction only. In respiration there is a "to and fro" current, which must modify the results somewhat. Experiments were performed with an artificial double current, but this does not reproduce the conditions of natural respiration as no absorption of vapour takes place, and the results are not of much value in consequence.

varying the area of the spread of the chloroform, contrasting strongly with that afforded by breathing "over" a less pervious fabric.

It is further a fact that variations in the rate of air currents produce far smaller changes in the percentage of vapour when passing through a fabric than when passing over it, probably because the air in every case is brought into very intimate relation with the chloroform.

The Mask, or Fabric, Inhaler.—We are now in a position to consider the practical application of the foregoing physical considerations to the use of fabric inhalers. An "open" mask such as the well-known "Skinner" is evidently not the most suitable pattern for regulation of the chloroform. It is usually covered with flannel and designed to be held some distance from the mouth, so that the inspired air passes largely *over* the chloroform; a comparatively large area of the fabric has therefore to be moistened with chloroform in order to obtain the requisite strength of vapour. The objections to its use may be stated as follows:—

(1) Successive douches of considerable quantities of chloroform being applied at intervals the temperature changes are appreciable.

(2) The inspiration being drawn *over* the fabric the vapour is not varied in proportion to the area moistened or in proportion to the number of drops applied.

(3) The maximum distance within which the mask can be removed from the face without attenuating the vapour too much is small, and it is difficult to make such fine adjustments of distance within this range as would be necessary for regulating the vapour.

It is in fact almost impossible to maintain with any approach to accuracy a constant level of anæsthesia by means of a Skinner's mask, but the results may be made of practical utility by acquiring the art of keeping the patient continually fluctuating between a state a little above and one a little below the required depth of anæsthesia.

The " perhalation "* method is far more amenable to regulation. A piece of domette is stretched on a light frame, the margin of which is shaped roughly to adapt itself to the contour of the nose and face, upon which it is allowed to rest, or retained in its place by very gentle pressure. The margin should be guttered to prevent liquid chloroform touching the skin.

With such a mask the strength of vapour may be readily adjusted by regulating the number of drops of chloroform applied and the consequent spread of chloroform. In order to avoid the effect of temperature changes the applications should consist of a few drops only at a time, and they should be made at intervals of a *given number of respirations* to ensure a constant vapour; intervals of *time* are useless, as the frequency of the respirations varies considerably. It is important likewise to ensure that the chloroform is fully evaporated before the next lot is applied, otherwise an accumulation of the residue will arise and result in a larger pool being formed than desired. The intervals of respirations must therefore always be sufficient, and the total evaporation of chloroform at the termination of the interval may be ascertained by passing a finger over the fabric, for a residue of chloroform affords a cold and damp sensation to the touch.

A safeguard against overdosage is introduced from the fact that the chloroform is soon evaporated (only just sufficient being used to last over a short interval of respirations), too soon in fact to produce overdosage even with the largest areas and a consequent high percentage in use, unless this be deliberately and frequently repeated.

A very large mask is unnecessary; it is probably disadvantageous, as it would enclose a large space in which no doubt the vapour would tend to accumulate

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* This term has been applied by Hewitt to the process of breathing through a fabric, but this principle would appear to have been first established by the author.

and upset the regulation. An exposed surface of about 16 sq. in. of a single fold of domette is fully sufficient (that is, a circle of $4\frac{1}{2}$ in. diameter or square of 4 in. by 4 in.). From such a mask rather more than 4 per cent. of vapour will generally be inhaled by human respiration from the whole area and slightly over 2 per cent. from half of it, but it is of course impossible to gauge the percentages accurately in such a relatively rough appliance. The mask need not fit absolutely accurately in the face, as the air entry through the fabric is so free that little comes under the edges; however, if the fit is very bad, naturally the vapour will be reduced in strength.

Every anæsthetist can work out his own method of regulation by drops in the way indicated, but the following routine constitutes a method which can be acquired with little trouble.

On a piece of fabric of the size indicated it is found that four separate patches of chloroform of 5 drops each may be applied without coalescing. Four grades of strength of vapour can be thus provided, but intermediate grades are readily produced by reducing the numbers of drops applied in one of the patches. The beginner will find it simpler, however, to work with the halves of the fabric only. Commencing with 2 drops of chloroform applied to one half every six respirations, the application is increased gradually up to 10 drops for the same interval. The process is then repeated *in addition* to the second half of the cover, but 15 drops in all (i.e., 10 drops to one half and 5 drops to the other), if applied repeatedly, will generally be found sufficient to induce anæsthesia, after which the percentage may gradually be reduced by reversing the process to the required extent. Thereafter any required degree of anæsthesia may be maintained by dropping a requisite number of drops at definite intervals, the percentage of chloroform remaining remarkably constant under such conditions.

An obvious change in the depth of the respirations

will necessitate some adjustment; that deeper respirations will require an increase of chloroform, rate being unchanged, and *vice versa,* is obvious. A change of *force alone* in inspiration may be neglected in this method.

The strength of vapour is not known accurately, and the administration is guided largely by clinical symptoms as to the depth of anæsthesia, but a certain knowledge of the relation between the number of drops used and the anæsthetic effect is acquired by practice.

This method may sound a little complicated in the description, but it is readily acquired, and soon becomes almost mechanical in its performance; it is capable of the double adjustment by varying the drops and intervals. It is the only method of giving chloroform on a mask which has any pretensions to precision, and it is the only one by means of which precise instructions can be given to students.

I have devised a cover of domette divided into segments of different sizes which each afford their appropriate strength of vapour, there being no necessity to observe intervals of respiration provided the applications are made sufficiently frequently to keep the segments constantly wetted, the chloroform being unable to spread from one to the other (fig. 6). This device should prove useful not only for practical purposes, but also as a means of teaching the value of areas.*

Percentage Inhalers.—Percentage inhalers are designed to regulate the strength of vapour by mechanical means, and at the same time to register the percentage of vapour presented for inhalation. None of them are entirely satisfactory, but the principles upon which they are constructed are of considerable interest. They may be classed in two groups: (*a*) The "Suction" or

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* Made by Allen and Hanburys, who also supply an approved pattern of frame.

"draw over," and (*b*) the "blow through" or "ad plenum" inhalers.

The Suction Type of Inhaler.—This type of inhaler* involves the use of a closely fitting face piece with its attendant discomfort and disadvantages. The nasal passages frequently become blocked by the pressure of the angle of the face-piece, and this leads to labial stertor and vibration of the valves of the instrument

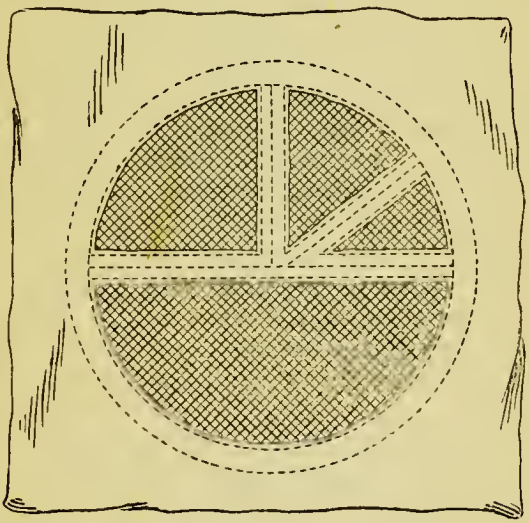

FIG. 6.—A cover for a mask, composed of segments of domette separated by a framework of batiste cloth. Diameter of circle 4 inches. When the sections are thoroughly wetted with chloroform the maximum vapour obtained by breathing through them is about 0·4, 0·8, 1·6 and 3·2 per cent. respectively, when the mask fits the face closely. Intermediate or excess values of vapour are obtained by employing the segments in combination.

unless the mouth is kept open; in edentulous people the sucking in of the lips may be troublesome. It is sometimes difficult to adapt a face-piece to fit closely, and any movement on the part of the patient adds to this difficulty; but unless adaptation is close pure air is drawn in under the edges and the adjustment of the

* Snow's inhaler may be taken as the archetype of this form of inhaler.

vapour is upset. These disadvantages are experienced during the induction stage; once, however, the patient is well under the anæsthetic and under control a free airway may be maintained by pressing the jaw well forward and the use of a mouth prop if necessary, and then it can be said that the results can hardly be improved upon. The sense of security and control are such as to render a long administration a somewhat monotonous performance, and, in the generality of cases, hardly calling for expert attention.

The principle of this type of inhaler is the splitting of the air current, so that part passes over the anæsthetic and takes up vapour and part does not, and by varying the proportions of the two currents by means of adjustable ports, the percentage of vapour inhaled may be controlled, and registered on a scale by an indicator.

The regulation of the vapour is a physical problem of considerable delicacy; an error of 0·5 per cent. of an atmosphere is not a great one from a physical standpoint, yet its physiological effect may be considerable. The chief difficulties to be dealt with are as follows:—

(1) The maintenance of the chloroform at a constant temperature.

(2) To combat the effect of variations in the force of inspiration upon the percentages of vapour.

(3) To stabilize the liquid chloroform. Owing to the high specific gravity and consequent inertia of the chloroform, any movement imparted to the container tends to wet the sides of the vessel to a considerable height and so increase the area of evaporation.

(4) The maintenance of the surface of the chloroform at a constant level from the aperture of air entry.

(5) To provide a perfectly free channel for the inspirations.

Suction inhalers are provided with valves* which cause the inhaled air to pass over a chloroform surface,

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* See appendix to this chapter.

and prevent reflux of the exhaled air; the latter passes out of a valved side-aperture in the mask.

The best known inhaler of this type is the Vernon Harcourt inhaler.* This is a rigid apparatus supported on a face-piece. It is provided with a stopcock with reciprocal apertures (so that one aperture is opened in the same proportion as the other is shut). In this way the total air inspired may be made to pass entirely over the chloroform or to do so in any proportion, and a pointer attached to the stopcock indicates on a scale the percentage of chloroform contained in the final mixture (fig. 7). Matters are so adjusted that when the whole of the air passes over the chloroform the vapour yielded should be at 2 per cent. concentration.

The chloroform container is a thin glass bottle with two necks like a Wolff's bottle, suspended from the intake tube by means of a rubber tube attached to one of the necks. The container is thus unstable, and a vapour of as much as 5 per cent. may be obtained when it oscillates freely; this is a serious fault,† which becomes accentuated if the patient moves during induction, and if the patient or the table is moved. Two glass specific gravity bubbles are adjusted, so that one just floats and the other just sinks in the liquid when the latter is at the required temperature, and this is maintained by the warmth of the hand, which is applied to the bottle as frequently as the behaviour of the bubbles indicates; this handling is in itself liable to produce an oscillation of the liquid chloroform.

The inventor claims that differences in the rates of the currents of air are compensated automatically, weak currents passing partly from inlet to outlet of the bottle without reaching the surface of the chloroform. This, however, is not the case, as may be demonstrated by

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* For a detailed description of this inhaler see the Report of the Special Chloroform Committee of the British Medical Association, and also Dr. Buxton's "Anæsthetics."

† Levy [9].

drawing a dense smoke through the bottle,* when it is found that even with the weakest aspiration vortex rings of smoke are propelled down to the liquid surface and there break up and circulate round the container; they never take the course assumed. Estimations of

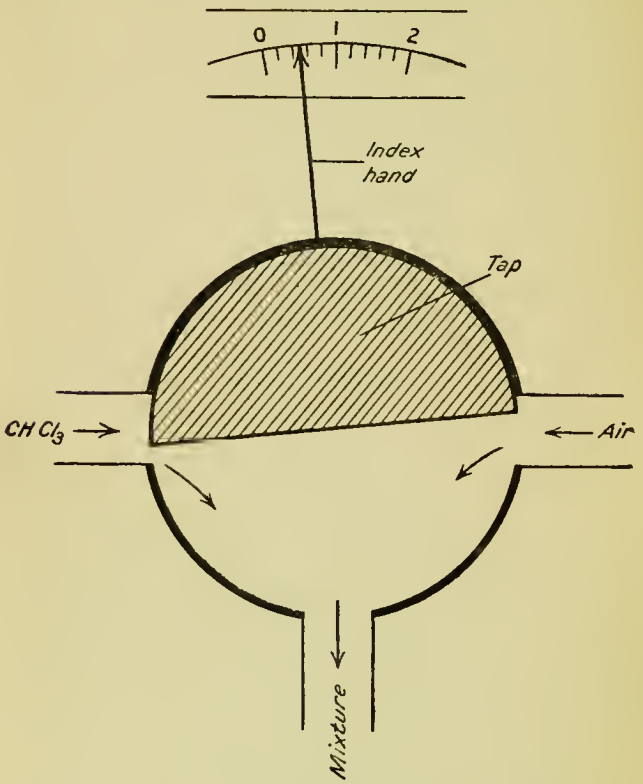

FIG. 7.—Diagram showing the principle of the regulating tap in the Vernon Harcourt inhaler.

chloroform obtained from this container show that even within narrow limits of variation of the air currents the variation of percentage is actually considerable; an illustration of this has been already given on p. 111.

* The cloud formed by uniting hydrochloric acid and ammonia vapours is suitable for this purpose.

The container is slightly conical in form, so that as the chloroform level sinks from evaporation the area presented becomes greater, and thus a measure of compensation is provided for the diminution of vapour caused by the lowered level.

The inlet of the container may be constricted by plugs, causing a more powerful jet of air to impinge on the chloroform, and higher percentages may be thus obtained, estimated at 2·5 per cent. and 3·0 per cent. respectively for the two plugs provided.

This apparatus is evidently by no means reliable as regards the evolution of vapour, and for many subjects, especially when the inspirations are strong, the strength of vapour provided is insufficient to produce efficient anæsthesia sufficiently rapidly without overheating the chloroform or agitating the container, but it is frequently efficient in maintaining anæsthesia thereafter. It does, however, evidently yield good results in the hands of administrators who are conversant with its peculiarities.

Levy [13] designed an inhaler with the object of avoiding the errors of the Harcourt inhaler (fig. 8). The chloroform container is a circular vessel surrounded by a water bath, which stands on a table and is not liable to agitation. The container is connected to the face-piece by means of a flexible tube. The pure air inlet is a relatively large aperture which is permanently open, and a stopcock regulates the proportion of air which passes over the chloroform in the container (fig. 9). Thus only a fraction of the inspired air passes over the chloroform, and as the velocity of such a fraction is relatively small, the disability of the varying force of the inspirations is partially compensated, for slow currents vary less in the amount of chloroform they take up according to their actual rate of flow.

It is necessary for the portion of air which passes over the chloroform to be highly charged with vapour, being considerably diluted by air coming in through the permanently open aperture, and for this purpose the chloroform is warmed by filling the water bath at a

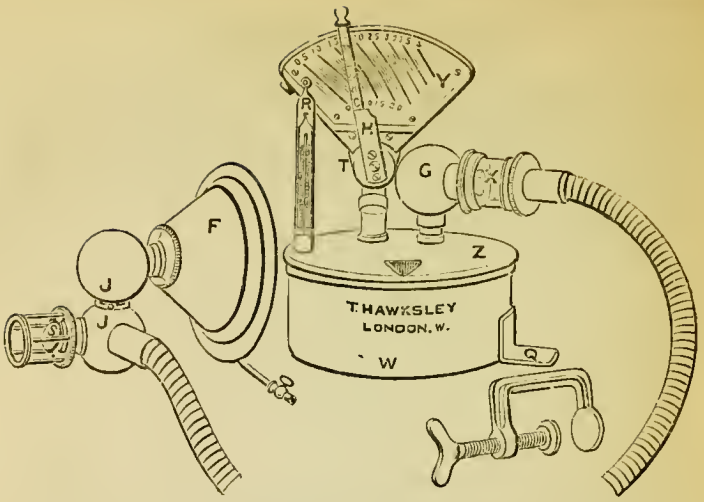

FIG. 8.—Levy's chloroform inhaler. F, Facepiece. J J, Double junction between facepiece and tube. S, Expiratory valve. X, Glass chamber containing inspiratory valve. G, Mixing chamber with air aperture (not sbown). Z, Cover containing chloroform chamber. W, Water bath. R, Tbermometer. T, Tap regulating chloroform supply (inlet not shown). H, Index hand. Y, Percentage scale.

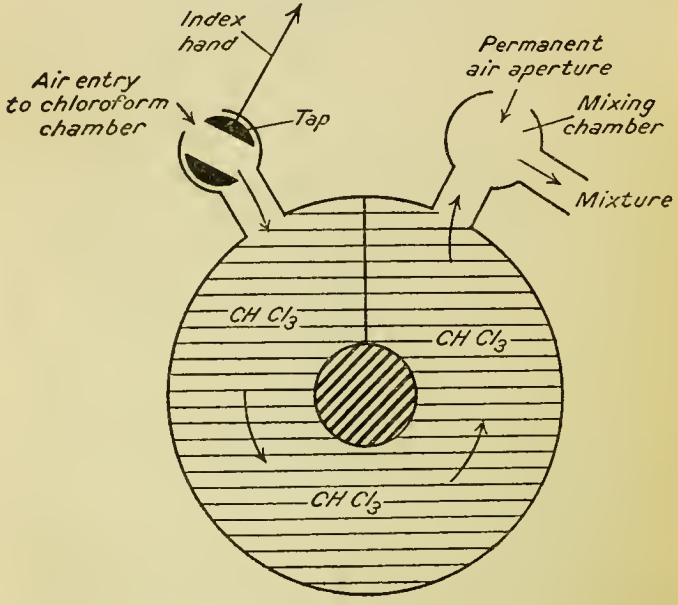

FIG. 9.—Diagram showing the course of the air currents in Levy's inhaler. The regulating tap controls that current only which passes over the chloroform.

temperature of 30° C. to 40° C. The index scale is provided with a temperature correction* which allows the percentage to be read off at any temperature of the water bath. The chloroform current passes through a series of tubes and passages, and in consequence undergoes a certain retardation (viscosity effect) which is not experienced by the pure air current coming in through the simple aperture; as the viscosity effect is more pronounced during weak suction, it follows that relatively more pure air is taken in during weak suction and relatively less during strong suction.† In this way a further compensation is provided which finally renders the percentages practically identical for all variations in the respirations; the size of the pure air aperture is so adjusted as to ensure this result. All the apertures and tubes of the apparatus are sufficiently wide to allow of very free respiration.

The apparatus is designed to deliver a maxmum of 4 per cent. vapour when the temperature of the bath is 40° C. This maximum percentage of vapour enables the induction to be carried out with fully sufficient expedition. The attachments to the face-piece are a little inconvenient, especially when the patient moves during induction, and might be modified. This apparatus is likewise inconvenient when anæsthesia is induced in a separate room, for then the administration has to be interrupted during transfer. This difficulty obtains with many forms of percentage inhalers.

Dr. C. T. W. Hirsch has designed a modification of a chloroform inhaler introduced by Dr. A. Waller.‡ It is by no means scientifically perfect, but it is claimed to be efficacious. The chloroform is contained for the most part in two cotton wicks, one coiled round the

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* The corrections were obtained by actual estimations throughout the scale of temperatures provided for. A simple sliding scale does not provide an accurate correction.

† Flow through a simple aperture is proportional to the square root of the driving pressure, whereas viscous flow is directly proportional to the pressure.

‡ Originally based on a design by Regnier.

inner wall of a cylindrical pot, and the other round the outer wall of a metal tube passing down its centre. The pot is connected by an angle-piece to a Barth's gas mask, and air is breathed in and out down the centre tube, there being no valves. A portion of the air, however, is drawn from the chloroform chamber through a bye-pass leading from the centre tube, and this chloroform current is regulated by an adjustable port in the cover which likewise communicates with the chloroform chamber, and to which is attached an index hand denoting percentages. Dr. Hirsch claims that the heat of the expired air regulates the temperature of the chloroform; a simple calculation will show that the heat of expired air, even if fully applied to this purpose, cannot compensate for the latent heat of chloroform abstracted by evaporation, but no doubt the expirations serve to prevent excessive cooling of the chloroform and so prevent an extreme limitation of the vapour. Any liquid chloroform which is in excess will evidently give rise to errors from movement, but this is no doubt kept in check somewhat by the absorbent nature of the walls of the container. Possibly there may be some inherent compensation for changes of respiration, but the apparatus does not appear to have been tested in this direction. The maximum nominal percentage is 2·5 per cent., which if correct is not sufficient; it is stated that perfect anæsthesia may be produced in fifteen minutes, which is too long a period for ordinary work. The apparatus appears to have been used mainly after a preliminary injection of morphia, and it is evidently efficacious in this combination. It is simple both in construction and application.

Hirsch strongly recommends the introduction of an "artificial air-way" for use in conjunction with the close-fitting mask after anæsthesia has been induced, and this is undoubtedly convenient in connection with all suction apparatus; the use of such a tube, however, requires a caution (see p. 143).

Ad plenum Inhalers.—With this type of inhaler the

patient inhales an anæsthetic atmosphere of definite composition, which is driven by a pump in a continuous current over the mouth and nostrils. It has the advantage of being a purely open method, for no portion of the apparatus touches the face, the funnel or face-piece employed to spread the outflow being merely approximated to the face. The breathing is unobstructed, the patient inspires exactly as when breathing ordinary air, and the respirations are appreciably stimulated by the current of air playing upon the face. It is a method which essentially lends itself to mechanical control of the strength of vapour, but a considerable flow of atmosphere is essential for success, and no doubt constitutes a difficulty.

To be efficient the rate of flow should satisfy the maximum rate of intake during inspiration which is likely to be encountered (see p. 54), otherwise pure air may be drawn in and further dilute the vapour. It is possible, however, that at abnormally increased rates of respiratory flow some dilution of the vapour may be not very material, being to a certain extent balanced under such circumstances by increased ventilation and absorption, and the minimum available output of an *ad plenum* inhaler may be empirically fixed at 500 c.c. per second (= 30 litres per minute). This system is, I believe, the best for percentage inhalers, but unfortunately no thoroughly efficient inhaler of this type has yet been constructed. Dubois designed an inhaler to afford a means of applying the principles laid down by Paul Bert. It is constructed on a good mechanical basis, but is heavy and costly, and does not supply a sufficient maximum of vapour.

The apparatus works on a double bellows principle, each expansion of the bellows taking up a measured quantity of chloroform. The current is maintained by turning a crank by hand, and it should be capable of meeting the requirements of inspiration, although this may easily become insufficient if the crank is turned too slowly.

The apparatus is graduated to supply three grades of vapour only, viz., 1·2, 1·6 and 2·0 per cent., with no intermediate stages, which is a disadvantage. At times the apparatus works consistently, but at other times, and without apparent reason, the percentages are somewhat erratic.

The nominal maximum of 2 per cent. is insufficient to produce full anæsthesia within the time limit of ten minutes, and the patient may be never properly under, as was the case in two administrations witnessed by the writer. On the other hand, Chapman has reported very favourably on the use of the instrument.

Alcock's *ad plenum* inhaler is compact and simple in construction, and it would appear that some such apparatus as this most nearly approaches what is required. The instrument embraces some of the principles of Levy's inhaler applied to the "ad plenum" system. It consists of a metal cylindrical chloroform container, in which only part of the air current passes over the chloroform through ports which can be partially occluded as desired. The temperature is controlled by a water bath, and a correction is made for temperatures between 60° and 70° F on a sliding scale. The motive power for driving the air is either a foot bellows or an electric fan, the instrument delivering constant percentages at current velocities between 8 and 10 litres per minute (= 140 c.c. and 333 c.c. per second). The maximum percentage obtainable is 3·5 per cent. This apparatus should be adjusted for a higher rate of delivery than 20 litres per minute, and the temperature correction should be extended to wider limits; it should then be efficient for the great majority of cases.

Waller's [2] "wick inhaler" provides a means of delivering a current of air containing percentages of vapour which vary according to the amount of wick exposed. It has no adjustments for regulating the temperature or compensating for the varied draughts, but the principle has practical possibilities.

The "ad plenum" method is adapted for intra-

oral or intra-pharyngeal administration, by means of a tube passed into the mouth, or through the nares. A special application is the intra-tracheal administration of chloroform which requires separate consideration.

Intra-tracheal Administration.—This method has the distinct advantage of ensuring a continuous ventilation of the lungs and abolishing the possibility of respiratory obstruction. A tube is passed through the larynx down to the bifurcation of the trachea, and the lungs are maintained in a state of continuous partial inflation by the internal pressure of the flow of anæsthetic atmosphere. The dead space is practically abolished, and the vapour diffuses continuously into the alveoli, so that there is a ready response to small changes of vapour tension, and the required effects can no doubt be obtained with lower percentages.

This method has considerable physical advantages in operations which involve opening the chest, and in operations upon the throat and pharynx, but it is one which, although excellent in connection with ether, must require considerable care with chloroform, for the administrator can no longer rely upon the proper performance of the respiratory function as a guide to the depth of anæsthesia. It is true it is not usual to maintain such a pressure as entirely abolishes natural respiration, but such respirations as survive must receive very close attention, and if suspended the question arises whether this is due to overdosage, excess of pressure, or to acapnia from excessive ventilation. It is obvious that a very careful watch over the respiration is required, together with an accurate method of regulating the percentages as a guide to the condition of the patient; it is possible to overdose the heart almost to the extinction of its beat with little asphyxial complication in this method of artificial respiration.

Pembrey states that an intra-tracheal flow of 30 litres a minute is liable to induce an acapnic condition and consequent cessation of natural respiration; a flow of 16 litres per minute only partially annuls respiratory

movements by its mechanical action, and as the alveolar CO_2 is then about normal, these partial respirations will continue. It seems probable that this lower rate would satisfy the partial respiratory requirements in intra-tracheal administration.

C. H. Mott has adapted the "Kelly" intra-tracheal ether apparatus for use with chloroform, and has obtained successful practical results. His procedure is to anæsthetize by an ordinary open method and maintain anæsthesia during introduction of the tracheal catheter, by vapour directed into the pharynx through a nasal tube; in this way there is no interruption of administration involved. The apparatus is evidently not sufficiently accurate as a percentage inhaler for use in this connection; Alcock's inhaler would appear to be more suitable.

Junker's Inhaler.—The well-known Junker's inhaler provides an anæsthetic atmosphere in *deficit* of ordinary respiratory measurements, so that the vapour must be delivered at a higher concentration than that at which it is to be inhaled, and it is diluted down by the excess of air drawn in by each inspiration. Presuming a delivery of vapour at a constant concentration, then the percentage of vapour actually inhaled is finally determined by the volume of the inspired air, which is not under the control of the administrator and can only be roughly guessed at. So long as the respirations are regular in volume, then the anæsthetic effect will be constant, but variations in the intake will at once effect a change in the anæsthetic effect; this will likewise be entirely different in individuals with different lung capacity.

A small continuous stream of air can be passed through the chloroform by partially closing the tap on the delivery tube, so that the elastic air reservoir is maintained in a distended condition by pumping; it is more usual, however, to employ intermittent streams of larger volume delivered direct from the hand pump. This intermittence requires accurate timing of the pump

to the moment of inspiration, otherwise the vapour is obviously wholly or partially wasted, and the anæsthetic effect produced in extreme want of synchronism is *nil*. This is such an obvious truism that it hardly appears worth mentioning, but the frequent neglect of this elementary principle in practice by students is remarkable. As generally employed there is no guide to the strength of vapour inhaled, and the pumping is adjusted according to clinical indications; a full squeeze or a partial squeeze of the pump every respiration, or every few respirations, as required. The delivery is generally regarded as a saturated vapour, that would be about 20 per cent. vapour at a temperature between 60° F. and 70° F., and it would appear from Waller and Well's estimations that this is so when the number of squeezes is few. If 100 c.c. be delivered by a single squeeze of the pump, and the inspiratory intake be 500 c.c. the vapour would be inhaled at 4 per cent. strength, and similarly in the case of a small inspiration of 300 c.c. the vapour would be 6·6 per cent. strength. The percentage of the delivery is, however, obviously subject to great reduction as the temperature of the chloroform falls from evaporation, according to the table on p. 109, and the temperature falls the more rapidly with more rapid pumping; when the quantity of chloroform in the container is small the temperature falls still more rapidly than when it is large. Thus with frequent pump compressions the percentage falls; doubtless also with a slow performance of the act of compression the vapour is more fully saturated than when it is performed quickly.* This apparatus is thus obviously one which it is difficult to control, although good results can be obtained by constant observation and practice. It is a convenient appliance for operations on the mouth and nose.

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* Kappeler's table in Hewitt's book appears to show this, but the figures given are difficult to understand ; on their showing the vapour would be supersaturated at the temperature mentioned.

In Krohne's modification of Junker's inhaler three different sized pumps are provided, of 10 c.c., 30 c.c., and 60 c.c. respectively; this provides a useful measure of control, but cannot provide even approximate percentages as the inventor claims. A mask is supplied with this apparatus to receive the vapour, and it has attached to it a balanced feather which moves with the respiratory currents and indicates the correct moment for pumping.

It is essential that precaution should be taken against pumping over liquid chloroform instead of vapour, as may happen if the pump be attached to the wrong end of the inhaler. Rigby's ball valve device appears to be a very suitable one for this purpose.

The Administration of Oxygen with Chloroform.—When a necessity for the administration of oxygen arises, in a case of extreme urgency it is no doubt permissible to take the risk of interrupting the administration of chloroform and concentrate on the relief of asphyxial symptoms. In less urgent cases the administration of chloroform must not be interrupted, and herein lies a difficulty. It is the usual practice to direct a stream of oxygen from a cylinder into the mouth through a small tube, which may pass under the mask or mouth-piece of the inhaler. This of course upsets the adjustment of chloroform vapour, and allowance has to be made accordingly. If the oxygen is not required in a large quantity a good plan is to resort to a Junker's inhaler, allowing the oxygen to bubble through the chloroform; this substitution of method can generally be rapidly made. Of course a flow of oxygen can be substituted for air in connection with ad plenum inhalers without upsetting the percentage; the oxygen is thus given pure, but the large quantity required would appear to be a disadvantage.

APPENDIX TO CHAPTER XI.

The Air-way of Apparatus.

Every piece of apparatus designed for use with a close-fitting face-piece should have an efficient air-way, that is to say, it must be capable of passing the respiratory current without effort on the part of the patient.

Insufficient Air-way.—It is doubtful if any apparatus is constructed with an air passage so small that it actually cuts down the air supply to a serious extent, for air can be drawn in sufficient quantity through a relatively small air-way with a slight extra effort, and no doubt for a short administration no great harm will result in this way; but a long-continued negative pressure set up by forced inspirations working against a resistance would cause some swelling of the mucous membranes throughout the respiratory tract, which would become detrimental by setting up internal obstruction.

Although the respiratory centre is capable of exerting a great continued effort when called upon, yet it does seem reasonable to conserve nervous effort as far as possible, especially in relation to such a vital function, and this is particularly to be considered in circumstances in which the respiratory centre is conceivably not working at its maximum potentiality. On these grounds it is advisable to secure a free air-way for all conditions of breathing.

Simple Apertures.—Any simple (i.e., thin-walled) aperture which is equal in area to the fully opened *rima glottidis* will certainly allow of a sufficiently free passage or air under all conditions. This area may be

estimated from the dimensions and figures of the larynx given in Quain's Anatomy to be approximately 150 sq. mm., which is contained in a circular aperture of slightly less than 14 mm. diameter, or in a square aperture of slightly more than 12 mm. It would be useless to enlarge the aperture further, and no doubt in practice a smaller circular aperture, of about 12 mm., diameter might be adopted if necessary.

Tubular Channels.—A tubular channel creates a considerable resistance to a current of air, the so-called "viscosity" effect, the resistance being increased in direct proportion to the length of the tubing. All tubes should therefore be as large as possible in bore. The smallest diameter of a short length of tubing should be 14 mm., the largest diameter likely to be required being 20 mm.; a tube of this latter dimension and 3 ft. long can be breathed through with perfect comfort, and this length of tubing is sufficient for most purposes. Deflections of a tubular passage and especially sharp bends add to the resistance, and should be avoided.

Valves.—Valves frequently offer some degree of resistance both to inspiration and expiration, by reason of moisture condensing upon them from the breath and setting up an adhesion to their seating. The greatest offenders in this respect are the wide thin rubber valves such as are employed in a "gas" apparatus, for they have a relatively broad overlap around the margin of the aperture of the diaphragm to which they are attached.

Hinged valves consisting of a disc of mica or aluminium are more suitable for prolonged administrations; they should rest upon a raised annular seating ground to a "knife-edge," otherwise the "stiction" from moisture becomes a serious difficulty. The Vernon Harcourt valve is counter-balanced, so that it can be constructed of thicker material which can be ground flat. Unfortunately these hinged valves must always be kept approximately upright, otherwise they will not operate efficiently. One way of avoiding this

difficulty is to provide a light spring over the hinge of just sufficient force to assist in closing the valve, but this is not entirely satisfactory. Another form of spring valve which has been employed is not hinged; a mica disc is contained in a perforated metal chamber, and lightly pressed in position by a spiral spring, but it is liable to jamb and requires watching. The valve to meet all requirements still remains to be invented.

CHAPTER XII.

The Administration of Chloroform. Clinical Considerations.

The preparation of the patient is for the most part on the usual well-established lines for a general anæsthetic, and requires no special comment.

Preliminary Alkaloidal Injections.—The preliminary injection of morphia is of doubtful benefit, although the patient is perhaps less prone to excitement under morphia, and no doubt comes more readily under the influence of chloroform. On the other hand, morphia tends to contract the pupil and obscures its reaction to chloroform, which is otherwise a valuable guide to depth of anæsthesia; it likewise tends to depress the respiratory centre, which is a serious objection to it. An extremely nervous or anxious patient may, however, pass through the induction stage more safely for a small dose.

There is little tendency to salivation under chloroform, so that a preliminary injection of atropin is unnecessary for the purpose of checking it. Its use has been extensively advocated as a prophylactic against sudden death from a presumed vagus inhibition of the heart, but in the light of our present knowledge of the pathology of sudden death it must be considered entirely useless in this connection.* Numerous instances have been recorded in which sudden death has occurred under chloroform, in spite of the prophylactic use of atropin; the general use of atropin is in fact to

* It may, however, be useful to restrain vagal action in such cases as require a continued extreme depth of chloroform anæsthesia.

be condemned, for it is safer to retain the full action of the vagal inhibitory centre. Vagal action diminishes the irritability of the ventricles; if vagal tone be abolished the ventricles are more ready to pass into an irregular tachycardia and subsequently to fibrillate.

The main principles involved in the administration of chloroform, and which have been already dealt with, may be summarized as follows:—

(1) To induce anæsthesia by a gradually increasing strength of vapour.

(2) To administer the vapour continuously from beginning to end of the administration; all unavoidable interruptions for cleaning out the mouth, &c., should be as brief as possible.

(3) Full surgical anæsthesia must be induced and maintained in every case.

(4) No more chloroform should be administered than is sufficient to maintain full surgical anæsthesia.

(5) A free air-way must be maintained throughout the administration.

In order to fulfil the foregoing conditions the experienced anæsthetist will no doubt employ the method with which he is most familiar and adept, but it will have been made evident that the more perfect the control over the strength of vapour which is afforded, the more easy and more perfect becomes the control of the various stages of anæsthesia. A really accurate percentage inhaler is not only a means of regulation of the depth of anæsthesia, but it provides, further, a guide to the effect desired, for within close limits a certain effect can be anticipated from a certain percentage of vapour. The mere progressive increase or decrease of the vapour can be compassed by any regulating inhaler, independently of the accurate registration of percentages, but it is performed with a regulating inhaler with an ease and precision which can be only approximately imitated by non-mechanical methods, and then only by much care and attention.

In non-regulated methods, and especially the douche

method, the vapour strength fluctuates over considerable periods, and as the administration must be efficient in respect of the point of lightest anæsthesia at any moment, it follows that the anæsthetic requirements are for a great part of the time exceeded; that is to say, the patient is subjected to a greater depressing influence than is necessary. When the vapour strength is controlled to a dead level the process of anæsthesia is a smooth one, and there is no necessity for overstepping the requisite degree of anæsthesia.

In the writer's opinion the best principle of regulating inhaler is that on the "ad plenum" system, provided the delivery is fully sufficient, and the best form of non-mechanically regulated method is the drop method described on p. 116.

The Induction of Anæsthesia.—The induction of anæsthesia presents two difficulties.

(1) *Restraint of Breathing* (p. 14).

This is often a troublesome occurrence, resulting in considerable delay in the induction of complete anæsthesia; further, if the supply of vapour is not regularly maintained by free inspiration during the stage of active absorption, the unsatisfied tissues rapidly deplete the blood of its chloroform, and thus the patient tends to "come round" when the breath is held.

A patient who "holds his breath" can generally be induced to inhale freely once more by slightly reducing the strength of the vapour, and the trouble vanishes entirely as he becomes progressively anæsthetized. Too strong a vapour at the commencement of inhalation may induce the patient to hold his breath, but, on the other hand, with an over-prolonged administration of a weak vapour a form of intoxication is produced in which the breath is held with great persistency.

(2) *Excitement.*

There is a strong contrast between certain classes of cases in regard to their liability to excitement. Domesticated persons generally exhibit little tendency, but robust and muscular persons, accustomed to vigorous

outdoor life, often give much trouble in this respect. Alcoholics are notoriously excitable under chloroform, whereas persons who have been enfeebled by illness are among the easiest to anæsthetize.

There can be no question that excitement during induction is reduced to a minimum when the induction of anæsthesia is performed by the delicate and gradual increase of the vapour from a low concentration up to the maximum, and it is even claimed that, provided the procedure is carried out with sufficient deliberation, any patient can invariably be anæsthetized without a single movement. This, however, is a counsel of perfection not always attainable, and at the same time it must be pointed out that it is not advisable to linger too long over this process, not only for reasons of economy of time, but likewise because during a prolonged period of partial narcotism a sudden outbreak of violent struggling may follow an accidental exciting cause; it therefore must be made a rule never to keep the patient too long on light percentages, and certainly never to decrease the vapour unnecessarily.

If, in spite of all precautions, much excitement or struggling takes place, it is most essential not to remove the chloroform if it can possibly be avoided; this is directly contrary to the old teaching, but the removal of the chloroform at this stage is a distinct danger. In order to continue the administration it is undoubtedly necessary sometimes to restrain the patient forcibly, for which purpose assistance is required. The patient's hands should be grasped by an assistant in the position of shaking hands, so that he cannot dash the inhaler away. As a general rule the excitement does not manifest itself in a tendency to struggle from the beginning, but struggling is often precipitated by a too early restraint of slight movement. If the patient shows a tendency to sit up even, he may be allowed to do so as long as he continues to inhale; he "loses himself" in the absence of resistance and generally soon peacefully subsides into the recumbent position, but he

may be roused to furious excitement by too early endeavour to force him back.

An animal may be quite safely anæsthetized by giving 2 per cent. or over from the beginning and forcibly restraining its struggles, but this method is obviously unsuited to man. A 1 per cent. vapour is comfortably respirable, but the greatest freedom from excitement is attained by beginning lower in the scale; the reason for this is quite obscure. Alcock recommends as a working rule the same numerical value for the percentage of chloroform as the time over which it is given, i.e.,

0·25	per cent.	up to	first quarter	minute
0·5	„	„	first half	„
1·0	„	„	first	„

and thereafter to proceed as the respiration allows. The sole guide for increasing the vapour is the respiration; it may be gradually increased so long as the respiration remains free. If the patient holds his breath it is useless to increase the vapour and better to reduce it, working up again as the respiration becomes free.

Signs of full anæsthesia may develop in five or six minutes in favourable cases; ten minutes is about the maximum time required. The indications of the approach of full anæsthesia are as follows: The respiration may become slightly stertorous in character. The pupils tend to become small, but not so small as in opium poisoning. The palpebral reflex tends to disappear; this reflex is evoked by lightly brushing the edge of the conjunctiva of the upper lid with the pulp of the finger, previously moistened with water or smeared with vaseline. The light reflex, obtained by alternately shading the pupil and exposing it to light, tends to become sluggish; both eyes should be shaded in performing this test. If these signs are delayed in appearance the strength of the vapour must be cautiously increased until the desired effect is obtained. The anæsthetist should then watch for signs of full anæsthesia. These are, a fixed eyeball, a *slightly*

dilated pupil, absence of palpebral reflex, a greatly diminished corneal reflex,* and a tendency to abdominal respiration. There should, in addition, be a total absence of muscular rigidity in all parts of the body.

There must be no sudden reduction to a lighter vapour following complete induction; the patient comes round with the greatest of ease at this stage (see p. 69), and therefore it is necessary very gradually to feel one's way back to a lighter strength of vapour whilst retaining all the indications of full anæsthesia. The percentages of vapour and quantities of chloroform required have been fully dealt with in Chapter IX.

It is particularly necessary to emphasize that the administration must not be interrupted during the transition from an anæsthetizing room to a theatre; if a non-portable inhaler is employed, then it is essential to provide means to carry on the process in some way during the transfer, and to allow no remission in the state of anæsthesia meanwhile. Any intermission at this stage is dangerous.

Nothing should be allowed to disturb the patient during induction. No dressings should be touched until the patient is completely unconscious and insusceptible to reflexes; in fact, he should be in a state of surgical anæsthesia before the nurse or surgeon be allowed to disturb him in any way.

The danger of the induction period has led some anæsthetists to induce anæsthesia with ether, or gas and ether, and then proceed to chloroform. At the moment of making the change the patient is coming out of ether and going under the chloroform, so there can be no clinical guide to the dosage of the chloroform. The chloroform should therefore be given and maintained in at least a full 2 per cent. strength, which is readily inhaled without excitement under such circumstances,

* Frequent testing of the corneal reflex undoubtedly injures the delicate corneal conjunctiva. This reflex is, however, a very valuable guide at times, and may be employed despite the slight after discomfort. It is not always quite reliable (see p. 142).

otherwise the patient will come round to some extent. The change is best made by means of an inhaler which supplies some indication of the strength of vapour.

There does not appear any serious objection to this method; it remains on trial, but there does not seem to be any particular advantage in it in ordinary cases, and the administration may as well be continued by the open ether method. I have found only a single record of death from this sequence in the Registrar-General's report.

The Maintenance of Anæsthesia.—When once full anæsthesia has been induced and the operation commenced, the administration resolves itself largely into the regulation of the chloroform to the appropriate vapour strength to sustain full anæsthesia in a continuous fashion.

The term full surgical anæsthesia is not quite a definite one; a degree of anæsthesia which is fully sufficient for many manipulations is insufficient for more severe ones. Severe manipulations, such as traction on abdominal ligaments, set up afferent impulses which rouse the central nervous system, so that reflexes return which were previously in abeyance. This is especially noticeable in the case of the corneal reflex, which returns, although the vapour strength has remained constant. It therefore devolves on the anæsthetist to anticipate stages of the operation by modifying the vapour accordingly.

The condition of the respiration should be carefully followed throughout the administration, for weakened respiration provides the first indication of impending overdose. The normal weakening of the thoracic movements may render it difficult to observe the state of respiration properly, and it is better in full anæsthesia to direct the attention to the abdominal movements. This is not always easy, however, in a patient who is well covered over, and some aid to observation is frequently desirable; thus, for instance, if a pair of pressure forceps or some similar long article be balanced

on the abdomen, its excursions will be found a distinct assistance in indicating the abdominal movements.

When the chest walls fall in with inspiration (p. 15) a confusion may arise between inspiration and expiration, and this is a matter of importance in certain methods of administration (e.g., by the Junker inhaler), in which an effort is made to time the administration with the inspirations; a misjudgment due to a cause of the foregoing nature will naturally lead to failure. In such circumstances the abdominal movements should be inspected, or the inspiratory and expiratory currents may be differentiated in a simple manner according to their difference in temperature by placing a hand near to the patient's mouth.

At the same time it is necessary to discriminate between weakened and actually obstructed respiration, and an indication may be afforded by the colour of the face, which may show signs of impending cyanosis. It must be remembered that an asphyxial condition may be the exciting cause of cardiac irregularities, especially if the administration be suspended during treatment of the condition; it is advisable, therefore, to keep up the administration of chloroform even during the recovery from a well-marked asphyxial phase.

The most general cause of respiratory obstruction is the "falling back of the tongue," and this is remedied by pressing the lower jaw forward, thus removing the base of the tongue from the back of the pharynx. If this should prove unsatisfactory the tongue should be held forward by forceps, or in cases of great difficulty by a ligature passed through the tip of it. In the case of edentulous persons the lips may be sucked in and cause an obstruction to inspiration, and then it is necessary to prop the mouth open either by a dental prop, or by a gag; sometimes a fold of towel inserted at one angle of the mouth is sufficient. A mouth tube curving down into the pharynx behind the root of the tongue, termed an "artificial air-way," is useful, especially in conjunction with mechanical apparatus.

It must, however, be used with caution, for it prevents swallowing; should anæsthesia become too light and vomiting occur, the vomit may be aspirated into the lungs.

The pulse should be kept under observation from time to time for abnormalities of the heart-beat; the occurrence of dropped beats should be regarded as indicating an irritable condition of the heart, and that the depth of anæsthesia should be gradually increased.

It is necessary to touch upon a certain condition which I have at times observed; it is not very common, but may become dangerous. The patient is not overdosed, a fair corneal reflex is present, the pupils are somewhat dilated, the skin pale and sweating; the pulse is rapid and small. This condition is the result of sympathetic reflexes from sensory stimuli under insufficient anæsthesia; it is generally regarded as one of shock, but it is not so in the proper sense of the word, for the blood-pressure may be well sustained. Should the anæsthetic be remitted during this condition a disaster might occur; the interests of the patient would be best considered by stopping the operation for a little while and putting him more deeply under the anæsthetic before proceeding further.

Narcosis should be properly maintained up to the last stages of the operation; in all except operations of long duration even during the final bandaging. When everything is completed the patient should not be "roused," but put back to bed with as little disturbance as possible.

For short operations chloroform should invariably be very fully administered, for cardiac syncope may occur during the rapid recovery which follows a brief administration of chloroform. In the case of children the danger is probably less, for they do not appear to be so subject to this form of syncope as are adults, but it is well even in their case to ensure very full anæsthesia before discontinuing the administration.

For operations requiring a light degree of anæsthesia,

chloroform is contra-indicated, and its employment is unjustifiable. Some other anæsthetic must be employed.

Ether may be advantageously employed in the course of chloroform anæsthesia for the purpose of stimulating the respiration should this have become weakened. A few drops of ether on an open mask will have a good effect under such circumstances; it is especially beneficial when the abdominal walls are slightly rigid in the course of an abdominal operation, although the patient is in other respects well under the influence of the anæsthetic; with the onset of free abdominal respiration the rigidity necessarily disappears. This administration of ether must be *in addition* to the administration of chloroform and under no circumstances used as *a substitute;* further, it should never be employed during the induction period, only after the patient has come well under the influence of chloroform.

The use of a warmed chloroform atmosphere has been strongly advocated, but it is difficult to conceive how any substantial benefit can be derived from it. The specific heat of air is so low that the extra heat supplied to the body is negligible. It is impossible to accept Gwathmey's contention that warm chloroform vapour is equally efficient as an anæsthetic agent but far less toxic; the conclusions can only be attributed to faulty experimental methods.

CHAPTER XIII.

Delayed Chloroform Poisoning.

Delayed chloroform poisoning is a rare and generally fatal condition affecting, for the greater part, young children. The following brief description of the symptoms is given by Telford and Falconer. "There is a striking resemblance in the clinical features of these cases. Vomiting, often severe and continuous, is seen in all of them, the vomited matter being in grave cases described as 'like beef-tea' or as 'coffee-grounds.' The patient's mental condition is changed. He may be drowsy, listless and apathetic, and the condition may deepen into coma before death. Air hunger, acetone in the breath and urine, and some degree of cyanosis are usually present. In the majority of cases the symptoms develop within thirty-six hours, and terminate within three or four days of the administration of the anæsthetic."

Information regarding the incidence of this affection is scanty; it appears for the first time in the Registrar-General's Report for 1919, in which eight deaths are attributed to delayed chloroform poisoning, and two deaths to "acidosis" in which the nature of the anæsthetic was not specified. The details afforded of the eight deaths are as follows:—

Ages	1 year	5 years	20 years	35 years	40 years
Male	1	1	1	—	1
Female	—	2	1	1	—

Total ... 8

The post-mortem findings are a fatty infiltration of the liver and generally some degree of fatty degeneration of the tubules of the kidney.

Serious attention was first directed to this condition by Guthrie, and according to him it occurs independently of the duration and depth of anæsthesia. Stiles and M'Donald later pointed out the similarity of the fatty degeneration of the organs to that which occurs in animals after the administration of chloroform, and these observations have been largely amplified by a number of workers in this country and America; it is perhaps an open question whether these changes do not occur in some degree in every case of the administration of chloroform and without symptoms. The distribution of the fatty degeneration is very similar to that found in men and animals as a result of sepsis (Apperley, and others), and a connection has in consequence been inferred between the conditions of sepsis and delayed chloroform poisoning.

There can be no question that animals (dogs, cats and rabbits) are very susceptible to a late effect of chloroform, and death is not uncommon a day or two after its administration. The symptoms in dogs are, according to Whipple and Sperry, identical with those found in man in delayed chloroform poisoning. In all animals the fatty degeneration of the liver is generally accompanied by a more or less extensive necrosis of the centre of the liver lobules, whether the termination is fatal or not; in non-fatal cases repair of the necrosis has taken place in two or three weeks' time.* It has been very generally assumed that a parallelism exists between delayed chloroform poisoning in man and the results obtained from experiments on animals, but it is pointed out by H. G. Wells that in the classical form of delayed chloroform poisoning, occurring mostly in children, the liver is not described as necrotic but as infiltrated by fat, and that there is another type observed, chiefly in young adults, marked by profound jaundice and the symptom complex of a rapidly fatal

* Graham suggests that the liver necrosis is due to the action of hydrochloric acid formed by the breaking down of the chloroform molecule.

acute yellow atrophy of the liver; anatomically the liver shows in such cases an extreme degree of necrosis.

A similarity between the symptoms of delayed chloroform poisoning and "acidosis" in children was noted by Brackett, Stone and Low, and their cases would further appear to show that a similar condition may follow the administration of ether; indeed, a condition of acetonuria is common in some degree after all operations (Beesly).

It is now the prevalent view that delayed chloroform poisoning is allied to the condition which presents the group of symptoms known as "acidosis," that the tendency is pre-existing and due either to sepsis or some form of malnutrition, and that the chloroform precipitates an acute form of the affection. In Buxton's opinion, some of the cases of death attributed to delayed chloroform poisoning have been really due to septic intoxication. On the whole it may be taken that the true relations of the disorder have not yet been definitely arrived at.

As arising out of the subject the folowing quotation, referring to work in the Children's Hospital, Edinburgh, is abstracted from Beesly's paper:—

"As the deaths described as due to delayed chloroform poisoning so clearly resembled the deaths occurring after operations with chloroform on children suffering from an acute infective condition combined with acetonuria, Mr. Stiles suggested using ether as an anæsthetic instead of chloroform. The results proved beyond question which is the best anæsthetic to use in such cases . . . Out of nineteen cases of acute appendicitis operated on under chloroform fourteen died . . . Out of twenty-four cases operated on under ether only two died, and that not as the result of acid intoxication."

This is a serious indictment of the use of chloroform in septic cases; so far as I am aware, it has neither been confirmed nor controverted, and it would appear highly desirable that this statement of Beesly's should be amplified by the experience of others.

The treatment of delayed chloroform poisoning is mainly the treatment of symptoms; the intravenous injection of a sodium bicarbonate solution, founded on the theory of an acid condition of the blood, is physiologically unsound, as shown by Bayliss. A rectal injection of a solution of glucose is given to all children before operation in some hospitals as a prophylactic against acidosis. According to Buxton, the chief indication is to maintain the strength of the patient until vomiting has ceased.

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